ETIOLOGICAL PROBLEMS IN UVEITIS

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Every ophthalmologist is able to settle the diagnosis of uveitis on the spot and he usually starts treating it immediately But in most cases this treatment will be purely symptomatic

We usually assume *that uveitis is an inflammatory* disease and at the same time we think of a reaction between some unknown *antigen* and *a specific antibody* This reaction sets free histamin like products causing inflammation Antiallergic drugs and steroids will certainly influence this reaction but will never reveal the etiology

Many attempts have been undertaken to demonstrate specific antigen in the diseased eye, be it bacterial, viral or a parasitic Positive *results for about every possible infective agent have been reported* in the literature, but mainly on enucleated eyes These findings are *very important for our knowledge of endogenous eye diseases,* but this kind of investigation did never have much clinical value The percentage of positive results is much too low, most cases remain unsolved problems

We have therefore paid more attention to the detection of specific *antibodies in the eye It must be said that despite the great work of A C Woods* there is no reason to believe that a specific infection in the eye *leads to an increase of specific antibodies in the blood or to* an increased sensitivity of the skin Very recent studies of *Hallett, Wollowicz, Fera, Leopold and Wyjewski* and also *of Coles* have shown, that blood tests alone (Middlebrook Dubos Test for Tbc, Antistrepto lysine O Test) are *of no value in the diagnosis of uveitis cases* It is therefore very strange that everybody still believes very much in the diagnostical value of the Dye test *(Sabin Feldmann)* for the detection of toxoplasmosis One should be aware that all these tests be it blood tests or skin tests can only be conclusive if they are negative Then at least we know, that this kind of infection is very unlikely to be the cause of an eye infection

We can assume *that for practical purposes,* a local antigen antibody reaction within the eye leads to a surplus of antibody This antibody will most certainly remain *fixed within the tissue But part* of it will leak into the blood stream, and part of it may get into the intraocular fluids (vitreous, aqueous humour) *If we can determine* these antibodies quantitatively within the blood, and at the same

time in the intraocular fluids, we may be able to find out, whether there is such a surplus or not It must be said however that one is more likely to find such increased antibody concentration in the aqueous humour in cases of exudative anterior uveitis, than in cases of rather mild posterior choroiditis

Antibodies are Gamma globulins We can therefore establish a correlation between the total gamma globulin content and the final titer of a serological reaction This ratio is called antibody activity If we compare antibody activity of the serum and of the aqueous humour we get another ratio which we can call antibody activity ratio Let us assume that all the antibody detectable in the aqueous humour of an inflamed eye were due to simple leakage of antibody through the damaged blood aqueous barrier then this ratio should be equal to one But if there really exists a surplus of antibody in the inflamed eye due to specific inflammation, then this ratio should be higher than one Very recent experimental studies of uveitis in rabbits after intraocular injection of crystallized ovalbumin have again shown that this hypothesis can be proven 10 to 15 days after the injection of the antigen a very marked infiltration with plasma cells and lymphocytes can be demonstrated in choroid and ciliary body By means of a hemagglutination technique the antibody activity in the aqueous humour can be shown to be higher than in the serum In a greater series of experimental leptospiral uveitis in rabbits the average antibody activity of the aqueous humour was three times as high as in the serum while on the other side non specific aqueous humour (secondary aqueous humour in systemically immunized rabbits) had an activity three times lower than in the serum Furthermore by using Coons technique with fluorescein labelled antibody it could be shown that the plasma cells in the iris and ciliary body contain specific antibody

In clinical cases of uveitis the situation is much more difficult since the antigen is unknown It is almost impossible to run more than three serological tests with the very small amount of aqueous humour available through puncture of the anterior chamber One has therefore to decide which antibody one should look for Our first studies were dealing with *tuberculosis* but we soon found out, that tuberculous uveitis is a very rare disease We never found a percentage higher than 8 and in later years it went down to 5 and even to 1 It may be that this rare incidence of tuberculosis in the eye is due to the fact that this infection is very much decreasing in our population But I am convinced that the diagnosis of *Woods* and others based on tuberculin skin test and the clinical picture were not true many of these cases probably never were tuberculous

Quite an amount of work has accumulated during the last ten years on ocular *toxoplasmosis* There is no doubt that the Dye test of Sabin Feldmann is the most reliable reaction so far used But one has to keep in mind that even for the Dye test the same thing is true as for all other serological tests a positive reaction in the serum of a

patient with uveitis does not by any means prove the toxoplasmic etiology of this inflammation, even if it presents itself under the clinical picture of a posterior central choroiditis There may be some reason to believe in a positive result only if — during the course of the disease — the titer of the reaction rises and later on drops down again when the local process is improving A definite proof of toxoplasmic etiology can only be given by our method of quantitative serology in serum and aqueous humour By means of this method we have found in a series of 217 cases a percentage of 7–10, which corresponds exactly with the results published by *Offret, Desmonts et coll* in France, using a very similar quantitative technique It is very interesting to note that proven cases of ocular toxoplasmosis with high antibody activity of the aqueous humour did not have high serum titers, but rather low ones This fact was also found by *Desmonts* and can perhaps be explained by an almost exclusively local (ocular) infection with toxoplasma In this case it is likely, that only little antibody leaks out into the blood stream, a little more gets into the aqueous humour, but most of it will probably remain fixed at the site of inflammation It must be mentioned however, that our method is not very sensitive and that we probably get negative results in cases, where only little inflammation occurs in the anterior part of the eye We most probably miss the diagnosis in many cases, where only old scars are seen without signs of activity

It seems that in Switzerland many people get infected with toxoplasmosis at an early age A small survey on 150 blood donors 18 to 22 years old gave positive Dye tests in 57% 20% had very high titers susceptible of fresh infection None of these young men and women had any clinical signs of systemic infection

As far as streptococcal infections are concerned, we come to the same conclusion as *Coles* and *Hallett and coll* we do not think that the Antistreptolysine 0 test is of any practical value in the diagnosis of uveitis We have not yet succeeded to work out a satisfactory micro method for the investigation of the aqueous humour We therefore have run this test only in the serum, but our results were very disappointing

It may be, that in so called rheumatoid uveitis, studies should be undertaken to demonstrate β2 A and M globulins in the aqueous humour and serum

These are our results of the last 2 years But I would like to say that there are numerous other infections possibly related with endogenous uveitis One has to think of nematodes, leptospirosis brucellosis leprosy, rickettsiae, viral diseases and many others

I have recently published a short paper on phaco antigenic uveitis, a very definite entity of autoimmune disease the diagnosis of which can be established by a specific hemagglutination It is very important that these cases — although clinically very similar — should not be taken as sympathetic ophthalmia They can be cured by intra

capsular extraction of the lens, which is not always to recommend in true sympathetic ophthalmia

I hope that I have been able to show how difficult the etiological diagnosis of uveitis really is It is therefore very unlikely that we ever will be able to know the cause of all our uveitis cases Because of these difficulties we have to treat most patients on a presumptive diagnosis But even if this treatment is often successful we should at least try to find out the cause of an endogenous uveitis Our method of quantitative serology is only one way to accomplish this very tedious task

SUMMARY

The quantitative determination of specific antibodies in the inflamed eye is one way to find the cause of endogenous uveitis In a positive cas the antibody activity has to be definitely higher in the aqueous humour than in the s rum Clinical examinations with this m thod have shown that tuberculosis has become a rare disease that significant toxoplasmosis titers were found in 7 to 10 per cent of the ases The micro-methods for the antistreptolysine-0 test in the aqueous humour are not y t satisfactory and have given disappointing results Many other infections may be th cause of endogenous uveitis and the possibilities of *quantitative serology* are not yet exhausted

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IRIDOSCHISIS AND PROGRESSIVE ESSENTIAL IRIS ATROPHY

A study of 20 patients with reference to the similarities in the clinical picture

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When reviewing the results of treatment of glaucoma associated with progressive essential iris atrophy and iridoschisis a marked overlap in the clinical picture was noted in two cases * Since then more data have been collected and altogether five combined cases have been encountered It is the purpose of this communication to present a short review of the entire series as well as to emphasize the diagnostic difficulties in the overlapping cases

MATERIAL

Cases with progressive essential iris atrophy (Table 1, cases 1 to 5)

Progressive essential iris atrophy is characterized by progressive atrophy and hole formation of the iris followed by displacement of the pupil The entire structure of the iris, the stroma as well as the pigment epithelium, appears to be involved by the atrophy (Figures 1 to 3)



Fig 1 Case 2, right eye



Fig 2 Case 1 right eye

Figs 1 and 2 Cases of essential iris atrophy

(*) Acta Ophth 39 356-366 1961

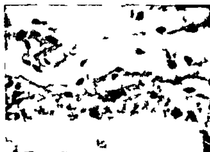


Fig 3 Case 19 left eye Essential iris atrophy A marked atrophy of the pigment epithelium as well as the stroma is noted



Fig 4a



Fig 4b

Fig 4c



Fig 4 Case 8 right eye with iridoschisis (a) before cataract extraction (b) following cataract extraction and (c) following discission of the iris membrane

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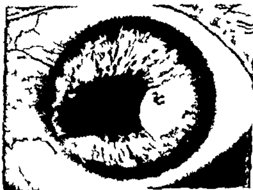


Fig. 1. Case 2, right eye.



Fig. 2. Case 1, right eye.

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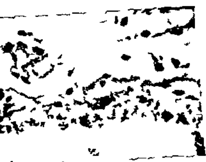


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FIG 4 Case 8 right eye with iridoschisis (a before cataract extraction (b following cataract extraction, and (c following discission of the membrane

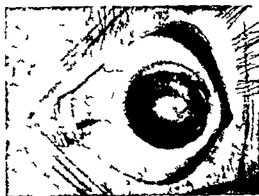


FIG 5 Case 9 left eye



FIG 6 Case 7, right eye

FIGS 5 and 6 Cases with iridoschisis



Fig 7a



Fig 7

Fig 7b



FIG 7 Case 12 right eye with iridoschisis (a) and (b) before and after an iridectomy, (c) histopathology showing leiomyoma of the iris



Fig 8 Case 16 left eye



Fig 9 Case 17 left eye

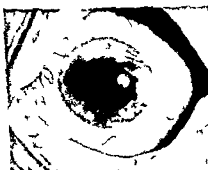


Fig 10 Case 18 left eye

Figs 8 to 10 Cases showing the characteristics of essential iris atrophy and iridoschisis

According to the literature however, the iris stroma is not detached from the pigment epithelium The process appears to be idiopathic not related to previous inflammatory conditions of the eye *Glaucoma* was present in six of the nine eyes with essential iris atrophy in our series

Cases with iridoschisis (Table 1 cases 6 to 15)

In iridoschisis a detachment of the iris stroma from the pigment epithelium takes place The stroma may be detached as a plane sheet or as separate strands (Figures 4 to 6) The changes are usually confined to the iris stroma the pigment epithelium not being involved by the process The condition may occur as an idiopathic atrophy where no cause to the stromal detachment may be found On the other hand there are cases with evidence of previous inflammatory or neoplastic condition The cases 9, 10 and 11 presented evidence of chronic uveitis To our surprise in one case (Table 1 case 12) iridoschisis was induced by leiomyoma of the iris (Figures 7a b c) The diagnosis was confirmed by the presence of myoglial fibrils in the cytoplasm of the tumor cells Two cases (6 and 8) were known diabetics

TABLE 1

ESSENTIAL IRIS ATROPHY

	Sex	*Age*	*Follow-up years*	*V A*	*Tonography*	*Chamber angle*	*Comment*
Case 1 Marked bilateral essential iris atrophy	Female	51	3 years	R E 0 6 *L E 0 35*	P_o - 6 mm Hg P_o = *13*	C = ? narrow C = 0 27 narrow	Cyclodialysis *1959* Cyclodialysis peripheral iridencleisis Iridencleisis 1959
Case 2 Slight essential iris atrophy in the right eye	Female	25	8 years	R E 1 3 L E 1 3 L E 1 3	P_o = 13 P_o = 13 P_o = *13*	C = 0 66 open (*closed* at the site of atrophy) C = 0 *66 open*	
Case 3 Marked bilateral essential iris atrophy	Female	50	2 years	R E 0 1 L E 0 4	P_o = 16 P_o = 15	C = 0 32 closed C = 0 37 open	Iridencleisis 1959 Retinoschisis Prophylactic Iridectomy 1959
Case 4 Bilateral essential iris atrophy	Male	77	*1 year*	R E 0 15 L E 0 55	P_o = *20* P_o = 22	*C = 0 17 open* C = 22 open	
Case 5 Bilateral essential iris atrophy	Female	55	1 month	R E 0 35 *L E* 0 25	P_o = 8 P_o = 17	C = 0 28 open with synechias C = 0 36 *narrow*	Acute glaucoma Iridencleisis 62

TABLE 1—*Contd*

IRIDOSCHISIS							
Case 6 Iridoschisis in the right eye	Female	61	2 years	R E 0 2 L E 0	P = 15 P = 80	C = 0 25 open C = 0 closed	Diabetic retinopathy cataract extraction 1959
Case 7 Marked iridoschisis in the right eye senile iris atrophy in the left	Female	[illegible]5	6 years	R E 0 08 L E 0 08	P_o = 9 P_o = 16	C = 0 28 not visible C = 0 [illegible] open	Iridencleisis 1935 *Iridectomy* 1945
Case 8 Marked iridoschisis in the right eye	Female	75	[illegible] years	R E 0 01	P_o = 14	C = 0 [illegible]0 open	Diabetic retinopathy Cataract extraction 1959 Discission of the iris 1959
				L E 0	P = 40	C = ?	Big scleral staphyloma
Case 9 Iridoschisis in the left eye	Female	55	2 years	R E 0 2 L E 1 00	P_o = 12 1 = 11	C = 0 32 not visible C = 0 33 not visible	Lipoid degeneration of the corneas
Case 10 Iridoschisis in the right eye	Male	3[illegible]	1 year	R E 0 5 L E enucleation for perforating injury 1959	P_o = 19	C = 0 20 open	Chronic uveitis

TABLE 1—*Contd*

IRIDOSCHISIS	*Sex*	*Age*	*Follow-up years*	1 1	*Tonography*	*Chamber angle*	*Comment*
Case 11 Iridoschisis in the left eye	Female	25	½ year	R E 1 0 L E 0	$P_0 = 14$ $P_0 = 0$	C = 0 31 open C = ? open	Iris blue Chronic uveitis from the age of 8 months Corneal diameter 9 mm Iris yellow brown
Case 12 Iridoschisis in the right eye	Male	22	½ year	R E 0 01	$P_0 = 16$	C = 0 26 open iris threads attached to Schwalbe s line in upper *nasal quadrants*	Iridectomy for congenital cataract PAD leiomyoma
				L E 1 6	$P_0 = 14$	C = 0 31 open	
Case 13 Marked iridoschisis in the left eye	Female	44	¼ year	R E 1 3 L E 1 3	$P_0 = 20$ $P_0 = 16$	C = 0 30 open C = 0 26 closed	Perforating injury in the childhood
Case 14 Iridoschisis in the left eye	Male	70	1 year	R E 0 L E 0 06	$P_0 = 17$	open with synechias	*Phthisis* Cataract extraction 20 years ago
Case 15 Iridoschisis in the right eye	Male	36	2 months	R E 1 0 L E 1 0		open with synechias open	

TABLE I *Contd*

CASES WITH FEATURES BOTH OF ESSENTIAL IRIS ATROPHY AND IRIDOSCHISIS							
Case 16 R E Essential iris atrophy L E Essential iris atrophy and iridoschisis	Female	65	2 years	R E 0 75 L E 0 6	P 14 P 6	C 0 25 narrow with synechias C	Cyclodialysis 1951 Cyclodialysis 1943
Case 17 R E Iridoschisis L E Essential iris atrophy and iridoschisis	Female	69	2½ years	R E 0 01 L E 0 2	P – 7 P 13	C – large open C – 0 21 open with synechias	Old choroiditis Iridencleisis 1960
Case 18 R E Iridoschisis L E Essential iris atrophy and iridoschisis	Female	73	4 years	R E 0 08 L E 0	P – 9 P = 66	C – 0 21 narrow but open C 0 closed	
Case 19 R E Essential iris atrophy and iridoschisis L E Essential iris atrophy	Male	71	1 6	R E 0 L E 0 55	P – 53 P 19	narrow with large synechias open	Cataract extraction 1959
Case 20 R E Essential iris atrophy L E Essential iris atrophy and iridoschisis	Male	33	1/12	R E 1 0 L E 1 0	P – 17 P = 17	C – 0 22 C – 0 27	
DYSGENESIS MESODERMALIS							
Case 21	Female	9	5	R E 0 2 L E 1 8	P 16 P = 53	C = 0 25 narrow with large synechias C 0 05 closed	Iridencleisis 1961



Fig 11a Case 21 right eye with dysgenesis mesodermalis The pupil has disappeared under the limbus at 11 30 o clock

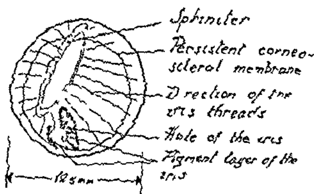


Fig 11b The same eye as in Fig 11a but four years earlier The pupil is slit like

Cases with the characteristics of essential iris atrophy and iridoschisis (Table 1, cases 16 to 20)

The overlap in the clinical picture was noted in five of the ten eyes of cases 16 to 20 (Figures 8 to 10) The opposite eyes showed either essential iris atrophy (cases 16, 19, and 20) or iridoschisis (cases 17 and 18) The overlap was confusing and rendered difficulties in the diagnosis The cause of the overlap is unknown One could assume however, that in essential iris atrophy the deeper layers of the stroma would show a more advanced atrophy resulting to the splitting As a matter of fact this probably took place in one case (number 19 In 1960 a marked iris atrophy was noted in the left eye without evidence of splitting Two years later definite iridoschisis had developed In iridoschisis on the other hand, the displacement of the pupil would require the pigment epithelium to be involved by the atrophy at the same time

As a differential diagnostic point a case with dysgenesis mesodermalis corneae et iridis is presented (Table 1, case 21) (Figure 11) This condition is often seen in children and is of hereditary nature, whereas no hereditary patterns were observed in the cases 1 to 20

According to the literature essential iris atrophy is mostly seen in young females whereas patients with iridoschisis are usually old In the present series four of the five patients with essential iris atrophy were females but both conditions were seen in young and old individuals without any clear cut predilection to age

ASPIRATION OF CONGENITAL CATARACT

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Aspiration of cataracts is an old technic, dating back to biblical times Refinements of the crude technics took place, until currently when aspiration is conducted manually and by motor suction It is the latter method which is featured in this paper Motor aspiration of congenital cataract has been carried on at the New York Eye and Ear Infirmary during the past three years The technic is as follows

PREOPERATIVE STUDY

The pupils are dilated maximally Those which do not achieve full dilatation require full basal iridectomy at time of surgery Others do well on one or two peripheral iridectomies Biomicroscopic study determines the size, nature and density of lenticular lesion, and any other anterior segment pathology, if present

SURGERY

General anaesthesia is used for all cases Narrow angle keratome section is made at the superior limbus The keratome penetrates directly into the lens nucleus, liberating lens matter into the anterior chamber The Kara aspiration needle, connected by tubing to a motor pump, is introduced through the same incision The needle is a specially designed, thin walled needle, 18 gauge with a 17 bore, flattened at the distal end and dulled at the tip The motor aspiration is controlled by a foot pedal The suction is calibrated at 40 cm Hg the aspiration is intermittent, under direct observation For better visualization of the cataract remnants during the aspiration the ultra violet light may be used The end point is a clear pupil, with a Ring of Soemmring behind the iris When this is achieved the iridotomy or iridectomy is performed, the wound is closed with one or two 6–0 chromic sutures, and air is injected into the anterior chamber Atropine, 1 per cent, is instilled These eyes are kept dilated for one month following surgery

With the zonular cataract, some modification of the technic is called for After the keratome section, the cystotome is introduced into the anterior chamber and the lens matter is stirred prior to aspiration The latter may be performed immediately, or forty eight hours later, if it is preferred to wait for full maturation of the cataract

The posterior capsule is usually peeled off the anterior vitreous face by this technic and coils away from the pupillary axis

DISCUSSION

The technic outlined above is essentially a linear extraction at one sitting In our hands it has been less traumatizing than the usual methods of management of congenital cataracts The surgery is of less than five minutes duration minimum intraocular penetrations are necessary the child is kept under general anaesthesia for a minimum period of time I emphasize this latter statement because I have witnessed congenital cataract surgery on infants which lasted one to one and one half hours

Thus far twenty five cases have been operated at the Infirmary according to the technic outlined above

Complications

Secondary membrane 2 cases Required discission Good subsequent postoperative result

Hyphema 1 case Resorbed, with no deleterious effects

Updrawn Iris 1 case Required sphincterotomy

Ages ranged from 6 months to 12 year Over half were under 5 years of age the vast majority having bilateral cataracts In four patients, the lens changes were hypermature, and bilateral surgery was performed a week apart

Vision

Because of the youth of the patients it was difficult to obtain accurate visual recording soon after surgery Gross approximations were made e g observation as the child picked up objects from the floor It is interesting to note that a corrected vision of 20/20 is rare after congenital cataract surgery The vast majority of patients achieve from 20/30 to 20/50 (even in uncomplicated cases!) This indicates that a cataract is merely one feature of an eye which may have multiple congenital aberrations e g poorly developed macula

Results obtained thus far encourage us to continue this technic until a large enough series, with a sufficiently lengthy postoperative follow up, is achieved so as to evaluate properly motor aspiration of congenital cataracts as compared with other methods of surgical treatment of this condition.

AN ESTIMATION OF THE REFRACTIVE INDEX OF THE HUMAN LENS IN VIVO

JIN OTSUKA, M D TAKASHI TOKORO, M D, MINORU ARAKI, M D

(Department of Ophthalmology of Tokyo Medical and Dental University)

INTRODUCTION

In physiological optics of the human eye, the crystalline lens is regarded to be a homogeneous refractive element and to have a constant value of the refractive index Under these assumptions, many diverse values of the refractive index of the lens have been adopted by many authors for phacometry, as shown in *Table* I

TABLE I

1 437	HELMHOLTZ
1 43	ZEEMAN, AUERBACH, TRON
1 416	SORSBY, YOSHIMOTO
1 41	TSCHERNING
1 409	TANI, OTSUKA TOKORO

Then, a series of experiments on the phacometry of the human lens and the ultrasonography of the eye was done *It was found that* the axial length of the eye determined by the ultrasonography did not coincide with the axial length calculated from phacometry using these previous values of the refractive index Such a *discrepancy must* be due to the assumptions inherited in phacometry, among which the assumption of the refractive index of the lens is the most fundamental Therefore, an attempt was made to search a new value of the most suitable index for physiological optics

METHOD

For this purpose we devised an apparatus for photographic phacometry and *for* ultrasonography (Fig I, Fig II)

For 46 normal *human* eyes from 9 to 21 years of age, 1% atropin *was used topically* in order to attain cycloplegia For these eyes, the axial length, the depth of anterior chamber and the thickness of the lens were measured by means of the ultrasonography The power of the lens was calculated using the refractive index of the lens of 1 409 for horizontal and sagittal meridians *The* axial length of the eye was then

calculated In performing the phacometry, Purkinje Sanson's images for both horizontal and sagittal meridians were obtained and therefore two values for the axial length of the eye were calculated Then, we averaged both values and regarded them to represent the axial length of the eye



FIG I



FIG II

COMPUTATION

The equation that is $l_P = F(r_1\ d_1\ d_2\ P_1\ P_3, P_4\ A\ n_k)$—(1) determines the relations of the refractive index of the lens and other optical constants (l_P calculated axial length for phacometry r_1, radius of the anterior surface of the cornea d_1, depth of the anterior

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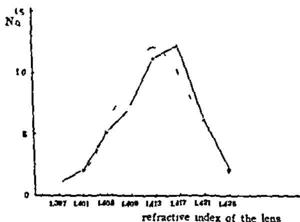
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On the other hand, the refractive power of the lens is fairly constant over whole range of refraction Therefore, it seems to be evident the change of the axial length is the most important factor in the genesis of myopia

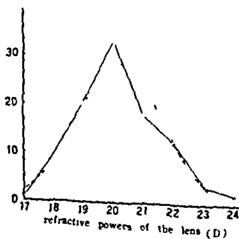
Fig III



average 1 413

standard deviation of ±0 006

Fig IV



average 20 21

standard deviation of ±1 39

chamber, d_2, thickness of the lens, P_1, P_3, P_4, distances of the Purkinje-Sanson's images, A, refraction, n_*, refractive index of the lens) When the refractive index of the lens is regarded to be a variable, the 11th power of function of n is obtained and it is very difficult to solve So we took a simple way for it

First, we assume $n_* = 1\ 409$ and put this value into the equation (1) and l_P is calculated

Next, we took a total differential of the equation (1),

$$dl = \pm \sqrt{\left(\frac{\delta l}{\delta r_1}\right)^2 (dr_1)^2 + \left(\frac{\delta l}{\delta d_1}\right)^2 (dd_1)^2 + \left(\frac{\delta l}{\delta d_2}\right)^2 (dd_2)^2 + \left(\frac{\delta l}{\delta P_1}\right)^2 (dP_1)^2 + \left(\frac{\delta l}{\delta P_3}\right)^2 (dP_3)^2 + \left(\frac{\delta l}{\delta P_4}\right)^2 (dP_4)^2 + \left(\frac{\delta l}{\delta A}\right)^2 (dA)^2 + \left(\frac{\delta l}{\delta n_*}\right)^2 (dn_*)^2}$$

where, r_1, d_1, d_2, P_1, P_3, P_4 and A are a small constant values and these errors are already estimated, that is, $r_1 = 7\ 7$ mm, $d_1 = 3\ 6$ mm, $d_2 = 3\ 6$ mm, $P_1 = 0\ 9$ mm, $P_3 = 1\ 8$ mm, $P_4 = 0\ 6$ mm, $A = -3\ 0$ dptr, $n = 1\ 409$, $dr_1 = \pm 0\ 003$ mm, $dd_1 = \pm 0\ 03$ mm, $dd = \pm 0\ 03$ mm, $dP_1 = \pm 0\ 002$ mm, $dP_3 = \pm 0\ 01$ mm, $dP_4 = \pm 0\ 002$ mm, $dA = \pm 0\ 25$ dptr Then,

$dl = \pm \sqrt{0\ 014055 + (-77\ 488)\ (dn)}$ —(3) is obtained $lu - l_P$ (lu, measured axial length for ultrasonography), that is dl, is regarded to be the errors of the axial length Therefore, the inferred index of $1\ 409 \pm dn$ is obtained and put this value into the equation (1) again and the axial length is calculated repeatedly until dl reaches to an infinitely small value Then, n_2 is calculated

RESULT

The refractive index of the lens calculated for 16 normal human living eyes averaged 1 413 with standard deviation of 0 006, when the accommodation is relaxed by the use of topical atropine and the distribution curve of the index proved to be binominal as Fig III

Using this value of the refractive index, we determined the power of the lens for 154 human eyes An average of 20 21 diopters with standard deviation of $\pm$ 1 39 diopters was obtained The distribution curve is fitted to a binominal curve as shown in Fig IV Moreover the axial length was computed therefrom

The whole sample was divided into classes according to their refraction and the power of the lens, the axial length and the power of the cornea were plotted for each class of refraction Connecting the average values in this plot, the curves were obtained as shown in Fig V The higher the myopia is, the longer the axial length

On the other hand, the effects of gamma angle in the phacometry were tested using model eyes which consisted of an optically grinded glass shell and a lens mounted with a metal ring and of an artificial anterior chamber filled with water in between them. The curvature of all surfaces and the refractive index of the material of the model eyes were known with accuracy Rotation of 5 degrees of the model eyes resulted in errors of less than 0 5% in the radii of the anterior and the posterior curvature of the lens This error makes a difference of the axial length of less than 0 003 mm which is considerably less than the accidental errors of the ultrasonography Therefore the neglected gamma angle makes no appreciable errors in the present calculation of the refractive index

Secondly, the refractive index obtained in the present study does not mean any true refractive index of the lens material, since the neglected posterior corneal surface alone can make the difference of 0 007 in the index The refractive index of the lens calculated without the neglected posterior corneal surface is higher than the case with the neglected one This consideration shows therefore that the neglected posterior surface is not the reason why we got higher refractive index than the Gullstrand s value For calculations in physiological optics most authors neglect the posterior surface of the cornea since it is very difficult to measure the curvature of it with accuracy So far as the physiological optics is concerned the present value seems to be valid and important

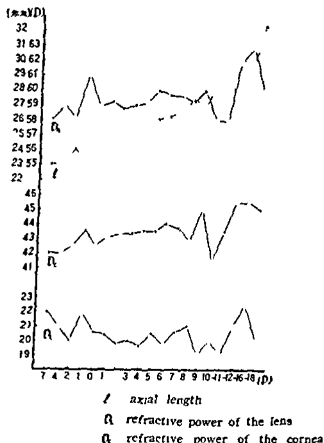
Thirdly, when we consider the accidental errors of phacometry and ultrasonography, the standard deviation was estimated to be 0 008 This calculation however was made assuming that the differences of the values for the axial lengths obtained by phacometry and ultrasonography were entirely due to the errors of the index If the deviation of the value for the neglected elements for example, the curvature of the posterior surface of the cornea non spherical anterior and posterior surfaces of the lens individual variations of the velocity of the ultrasonic waves in the media etc were taken into account the actual deviation of the refractive index may become smaller Sorsby mentioned in his studies on emmetropia and its aberrations that the deviation of the total refractive index of the lens seems to be negligible in calculating constants of optical elements of the eye The deviation of the index obtained by our experiment was less than 0 008 and this result may offer a very good evidence in support of Sorsby s statement

Sorsby also mentioned that the axial length calculated from phacometry were shorter than those measured with X ray vision In the present work the calculated axial lengths in phacometry were longer than that measured with ultrasonography The reason why we have got an opposite result to that of Sorsby is probably due to the fact he used the higher value for the refractive index of the lens that is 1 416 than 1 409 which was used in our calculation The present refractive index of the lens 1 413 may therefore be used as the most

DISCUSSION

The assumptions set in phacometry are that the gamma angle and the posterior surface of the cornea were neglected and the crystalline lens was regarded to be homogeneous These assumptions will now be discussed

Fig V



l axial length

R refractive power of the lens

R refractive power of the cornea

First, the phacometry was performed with regard to the optical axis of the eye, while the ultrasonography was done with regard to the visual axis The difference between two axes, that is, gamma angle was neglected Changes of the corneal curvature, when the eye is rotated around 5 degrees, that is, an average value of the gamma angle, were shown by Noto to be less than 0 01 mm which leads to a difference of only less than 0 06 mm of the axial length by calculation According to Tornquist the difference of the values of these axes make only negligible difference in the measured depth of the anterior chamber The centre of the rotation of the eye locates near the posterior pole of the lens and therefore the neglected gamma angle should not make any appreciable errors in the measurement of the lens thickness

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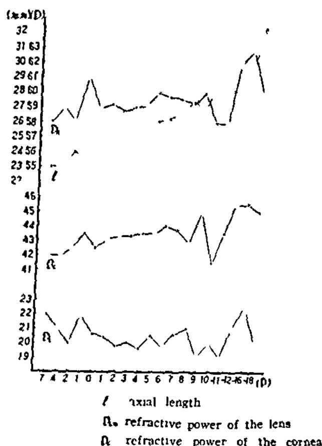
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Fig V



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PRODUCTION OF CATARACTS BY THE INTRALENTICULAR INJECTION OF ENZYMES AND ENZYME INHIBITORS

SHOCH, D., VAIL, D. and ZELLER, E. A.,
(with the assistance of E. A. Andujar), *U.S.A.*

The lens epithelium appears to be the major target of most chemical and physical agents which have been used previously to produce experimental cataracts. Recently we developed a new procedure by injecting *in vivo* certain compounds directly into the lens and thus bypassing the epithelium (XVIII Consilium Ophthalmol., abstracts, p. 713). Thus far two classes of substances, haloacetates and proteases, have turned out to be effective. To gain some insight into the action of these cataractogenic substances, the sequence of morphological changes which appeared after the intralenticular injections were followed. In addition, certain facets of the protein metabolism of the opaque lens were investigated, e.g. by determining the protein and non protein content and the aminopeptidase activity. Into one eye of rabbits 2.5 μ moles of iodoacetate or 25 μ g of crystalline papain were injected while the other eye received the solvent alone. Statistical analysis of the results obtained after 10, 20 and 30 days revealed that the administration of iodoacetate was more efficient than that of papain in reducing protein content and peptidase activity. In neither case was the loss of protein compensated by higher non protein values.

ABNORMAL PROTEIN METABOLISM AS THE CAUSE OF DEVELOPMENT OF CATARACT IN OCULAR LENS*

ANIMA DEVI, Ph D

Department of Biochemistry, Faculty of Medicine,
Laval University, Quebec *Canada*

If the development of cataract in ocular lens is the result of an accumulation of denatured protein it is possible that it has been caused by a progressive loss of hydrolytic activity of inter and intra cellular proteases in the lens The mechanism of protein synthesis may also be impaired so that these intracellular cathepsin like enzymes, so vitally important in removing the denatured proteins, are not synthesized to the extent as necessary Whatever may be the cause of the development of cataract it can be said that it is in some way connected with a defect or defects in protein metabolism In the present communication I would like to discuss this aspect of protein metabolism which appears to be responsible for cataract development

The ocular lens as we know, contains the highest percentage of protein than any other tissue of the body and is mostly made up of an albumin like protein To maintain the transparency, the lens must have a very active mechanism for the removal of denatured proteins as well as for the synthesis of proteins in other words there should exist a dynamic equilibrium between the processes of protein anabolism and catabolism in lens if the transparency of the lens is to be preserved Any abnormality in any one of these two processes should lead to the development of cataract

The importance of intracellular proteolytic enzymes in the development of certain types of cataract was first recognized by Borden Cooper (1) Goldschmidt (2) and others (3) as far back as 1914 and 1925 although definite evidences first appeared from the work of Zeller and Devi (4) These investigators reported that they observed a gradual loss of proteolytic activity of a chymotrypsin like enzyme in the lens during the progressive development of cataract induced by x rays

The autolysis of lens proteins was first noted by Clapp (5) and extensively investigated at a later date by Krause (6) Zeller and Devi (4) in their studies used manometric methods for the measurement of protease activity in lens homogenate The method was based on the liberation of CO_2 by the enzymatic hydrolysis of synthetic

( ) This work has been supported from a grant (no MA 1267) received from the Medical Research Council of Canada.

amino acid ester in a medium containing $NaHCO_3$. From the substrate specificity studies and studies involving the use of specific inhibitors of different known *proteolytic enzymes Devi (7) finally succeeded* to characterize the enzyme. It is, according to her findings, an enzyme very similar to chymotrypsin and has been designated as a *cathepsin C like* enzyme.

In recent years, several studies of the hydrolysis of proteins by proteases of various tissues have led to the discovery of more than one pH optimum, a finding generally interpreted as an indication of the presence of more than one protease (8, 9). Continuing the previous work on proteases in *lens*, Devi (10) recently demonstrated the presence of three pH optima, widely separated, *in the pH activity* curve resulted from the digestion of urea denatured hemoglobin or *serum albumin by bovine lens homogenate over a pH range of 3.0 to* 10.0 (Fig. 1). The variations in the ability of lens homogenate to

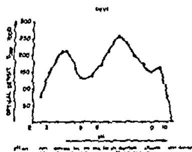


Fig. 1

hydrolyse urea denatured hemoglobin at different hydrogen ion concentrations are shown in this figure and from the three different pH optima, the author *concluded that there are at least* three different proteolytic enzymes in the lens, *if not more*. In these experiments fresh *bovine lens homogenate* as the source of enzymes and urea denatured hemoglobin and *serum albumin were used* as the substrate between pH 3.0 to 7.0 and 7.0 to 10.5 respectively. The conditions of the experiment employed in such studies are shown in Table I.

TABLE I — *Experimental Conditions for the Measurement of Protease Activity of Lens Homogenate*

(1) 1.0 ml of 6.0% solution of urea denatured hemoglobin or bovine serum albumin made in 0.1 M buffer

(2) 1.0 ml lens homogenate (70 mg of protein/ml)

(3) 1.0 ml buffer of 0.2 M and different pH values

Time of incubation — 2 hours

Temperature of incubation 28 C ± 0.5 C

The enzymes were then identified by subjecting the clear supernatant fluids obtained after centrifugation at 0 C at 16 000 r p m of the incubated reaction mixture to a descending chromatographic analysis. Enzymes optimally active at pH 3.8 and pH 7.0 were found to be similar to pepsin and chymotrypsin, no trypsinlike enzyme was detected, nor it was possible to identify the enzyme acted optimally around pH 8.5 to 9.0. This enzyme was not however identical with carboxypeptidase as no hydrolysis of a specific substrate for carboxypeptidase by lens homogenate was detected under the experimental conditions. The results of chromatographic analysis are illustrated in the Table II. The details of this experiment have previously been described by Devi (10)

TABLE II — Characterization of Proteases in Bovine Lens

Substrates	*Buffer used*	*pH range in which the reaction was carried out*	*Reagent used to develop colour of chromatograms*	*Coloured spot*	*Enzyme suspected*
Carbobenzoxy-l-glutamyl-l-tyrosine (for pepsin)	Acetate	3.0–5.0	Ninhydrin for tyrosine	Gray bluish	Pepsin like
N-acetyl-tyrosine ethyl ester for chymotrypsin	Phosphate	5.6–7.5	Pauly reagent for tyrosine derivatives	Orange brown with different Rf values 0.9 0.2	Chymotrypsin like
Benzoyl-l-arginine methyl ester for trypsin	Phosphate and glycyl glycine	6.0–8.0	Sakaguchi reagent for Arginine derivative	No coloured spot	No trypsin like enzyme

These findings although clearly demonstrate the importance of intracellular proteolytic enzymes (cathepsins) in maintaining the transparency of the lens do not tell us whether or not the gradual loss of proteolytic enzyme activity is caused by the inability of the lens to synthesize these enzyme proteins or is due to the denaturation of enzyme proteins. Recently Devi and associates succeeded to demonstrate the presence of an active amino acid incorporating system in rat lens (11). Based on the results derived from the in vitro experiments, it appears that the rat lens incorporating system is several times more active than the rat liver incorporating system of the same animal. This incorporating system is 10–12 times more active in the presence of 5μ moles of Co^{++} than in the presence of the same amount of Mg^{++}. These results are summarized in Table III. Co^{++} can not be replaced by any other metal nor even

TABLE III — *Incorporation of C^{14} Leucine into Lens RNA protein complex*

Counts per minute per mg of RNA protein complex			
	In presence of Mg ++	*In the presence of Co ++*	
Complete system	*51*	Complete system	49.
— Mg	16	— Co	*16*
— ATP	12	— ATP	466
— GTP	36	+ GTP	408
+ *Chloramphenicol (100 g/ml)*	49	+ Chloramphenicol *(100 g/ml)*	478

*by Ni which resembles Co++ in many respects Ni++ inhibits the incor*poration of amino acids into RNA-protein complex (11, 12) Many reducing agents such as cysteine, glutathione, ascorbic acid etc *have been* also *recently found to inhibit the incorporation of* C^{14} Leucine into TCA insoluble material Addition of EDTA has been found to be equally active in suppressing the incorporation of C^{14} Leucine These results are shown in Fig 2

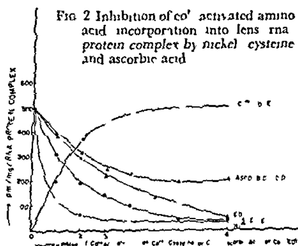


FIG 2 Inhibition of co' activated amino acid incorporation into lens rna *protein complex by nickel cysteine* and ascorbic acid

It has been found (13) that if the TCA precipitable material (in 5 ml of 5% TCA) is heated at 90°C for 15 mins about 75–80% of the total counts previously noted disappear *which suggests that only one fourth* of the total incorporated amino acid is retained by the proteins and obviously the remaining portion was incorporated into RNA Chromatographic analysis of the extract obtained by heating the TCA washed residue in 10% NaCl solution at *100 C* for 30 mins,

shows that the C^{14} amino acid remained with the RNA at the origin of chromatogram which might be considered to indicate that the amino acid is truly incorporated onto the RNA. Further evidence was obtained when the NaCl extract (RNA ~aa complex) was hydrolysed in 6 N HCl and then subjected to chromatographic analysis as before The radioactive spot was detected at the position corresponding to Rf value of free leucine used as a reference substance

The acid insoluble material used in this experiment was obtained after centrifuging the incubation mixture to which an equal volume of 5% TCA was added The incubation mixture contained 5μ moles of C^{14} leucine (0 9 × 10^{5} c p m) 50μ moles of tris buffer pH 8 5 2 5μ moles of ATP 25μ moles of Co^{++} and 2 5 ml of lens homogenate 50 mg ml of the solution

The Co-activated amino acid incorporating system of rat lens is truly an enzyme catalysed reaction and not merely a reaction involving RNA amino acid and Co as in the experiment where C^{14} leucine was incubated in the presence of yeast RNA or rat liver soluble RNA and Co^{++} with and without albumin hardly any radioactivity was picked up by the TCA precipitable material The fact that Ni strongly inhibits the incorporation of C^{14} leucine into acid insoluble material also leads to the same conclusion. Above all a three to five fold increase in hydroxymic acid formation occurs in Co-activated incorporating system should be considered as an additional evidence in favour of the enzymatic reaction (12)

If it is a fact that any disturbance in protein metabolism might induce the development of cataract then one would expect an abnormality in protein metabolism in ocular lenses of galactose fed rats since it is known that the feeding of a high galactose diet to young rats results in the development of cataract in their lenses (14 15) Whether or not protein synthesis in such lenses is also affected was tested by their ability to incorporate C^{14} amino acid into RNA protein complex (16) A significant decline in the incorporation of C^{14}

TABLE IV — *In vivo incorporation of C^{14}-amino acid into lens proteins of normal and galactose fed rats*

	Counts min mg of acid insoluble material			
	Normal rats		Galactose-fed rats*	
	4 hrs.	16 hrs	4 hrs.	16 hrs.
C^{14} leucine	12 4	5 0	6 0	4 3
C^{14} valine	14 5	6 0	8 5	3 0

* Data presented are the average of 5 such experiments. The animals were sacrificed at 4 and 16 hours after the injection of C^{14} leucine for experimental details see the text

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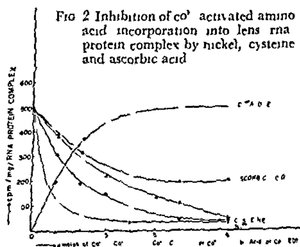


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C valine	14 5	6 0	8 5	3 0

Data presented are the average of 5 such experiments. The animals were sacrificed at 4 and 16 hours after the injection of C leucine for experimental details see the text

into lens proteins of such animals was noted when C^{14} amino acid was administered *intraperitoneally* into rats 4 and 16 hours prior to death. The results are shown in Table IV. But when the incorporation experiments were carried out *in vitro* with lens homogenates of such animals in the presence of ATP, Co^{++} (or Mg^{++}), C^{14} leucine etc. no significant reduction in the incorporation were noted as shown in the Table V. The reason for the difference in the results of these

TABLE V — *In vitro incorporation of C^{14} amino acid into lens protein of normal and Galactose fed rats on the presence of Mg^{++} and Co^{++}*

	Counts/min/mg of acid insoluble material			
	Normal rat*		Galactose fed rat*	
	Mg^{++}	Co^{++}	Mg^{++}	Co^{++}
C^{14} leucine	26.8	520	24.8	500
C^{14} valine	18.5	610	16.8	590

* Data presented are the average of 5 such experiments, for experimental details see the text.

two types of experiments might be due to the unavailability of ATP in the former (*in vivo*) experiment and the presence of sufficient amount of ATP in the later case (*in vitro* experiments) as ATP was added externally. ATP is required for protein synthesis, without it amino acid could not be activated and as far as we know today, this is the initial step in protein synthesis (17, 18). We also know that in fully developed cataract the concentration of ATP is very low (19).

From the recent study by Devi and Passi (20) it reveals the fact that both ATP and DPN concentrations are progressively decreased with the gradual development of cataracts. Cataracts are induced by high galactose diet as well as X rays. Nearly 50 per cent of the initial ATP concentrations appears to be lost with a visible sign of lenticular opacity (observed under biomicroscopy). The decrease in ATP concentrations is further progressed with the extension of opacification and finally a complete disappearance in fully matured cataract is observed. Lens is apparently devoid of ATPase activity with the exception of that in a very superficial layer of epithelial cells; the disappearance of ATP during the development of cataract appears to be due to the impairment of synthesis of ATP itself since no appreciable increase in ATPase activity has been detected in the cataract. That ATP generating system in the lens of rats with high galactose diet is seriously disturbed, has also been noted from recent investigation (21). It is to be noted here that a complete disappearance of ATP in all types of senile cataract supports the view that an interference of protein synthesis during progressive development of cataract occurs. High energy phosphate bond is indispensable for activating amino acids before the peptide chain is synthesised on a RNA template.

The unavailability of ATP in galactose induced cataracts seems to be therefore the real cause of decreased protein synthesis

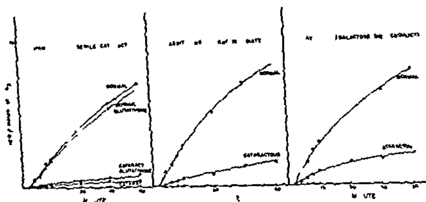


Fig 3

Do we also find a concomitant loss of proteolytic activity in galactose induced cataracts? In order to know this the determination of proteolytic activity of the lenses of such animals was undertaken A progressive loss in proteolytic activity was noted during the gradual development of cataract in fact a loss of 70–90 *per cent activity* was found in fully developed cataracts in senile cataract and cataracts induced by either X rays or by feeding diets containing galactose as shown in Fig 3

Thus a complete loss of proteolytic activity in the fully developed cataracts is observed in all cases as shown in this figure It does not matter how it is caused

Although it appears that the loss of proteolytic activity is the real cause in the development of cataract nothing is known why the activity is progressively lost during the development of cataract Is it due to the impairment of protein synthesis in the lens resulting in the decrease of the protease concentration that is not known We do however know that the ATP concentration is greatly reduced which might interfere with protein synthesis In any case it appears that the development of cataract in one way or other is caused by a defect or defects in protein metabolism possibly in protein synthesis and more precisely in the synthesis of enzyme (proteolytic) proteins It is not the end of the work rather appears to be the beginning of our research for the primary cause which interferes with the mechanism of protein synthesis Our laboratory is actively engaged in such work The knowledge we expect to gain through researches will be of immense value in preventing and curing this disease

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L'IMPORTANCE PRATIQUE DE L'EXAMEN DE LA FONCTION VEGETATIVE DE LA RETINE

M. RADNÓT ET E. WALLNER
Budapest, (Hongrie)

La lumière provoque une eosinopénie sur l'individu normal. C'est ce qui se reflète dans le sang par l'oscillation journalière des cellules eosinophiles. Si ces mêmes individus sont soumis à l'obscuration le nombre des cellules eosinophiles reste invariable (1). L'intensité de l'eosinopénie causée par la lumière s'approche de celle observée à l'épreuve de Thorn à la suite de l'application de l'adrénaline ou de l'ACTH. Le fait mentionné ci-dessus peut être attribué à l'activité du système hypophyso-surrénal et peut être enregistré comme une manifestation de la fonction opticovégétative.

Au point de vue théorique et clinique il y a intérêt à examiner quelles maladies de l'oeil peuvent influencer l'effet de la lumière de l'eosinopénie normale. Nous avons pu établir dans le materiel examiné que les opacités de la lentille et du vitre n'y exercent aucune influence même si l'acuité visuelle baisse considérablement. En cas de dégénération pigmentaire de la rétine aussi là où le rétrécissement concentrique du champ visuel s'est réduit à 5–10° la lumière provoque une eosinopénie normale. Par contre le centre de la rétine intacte est la condition primordiale de l'effet végétatif de la lumière. *En cas d'une degeneration de la macule* là où la périphérie se trouve intacte mais le centre comporte des altérations l'effet de la lumière ne provoque pas d'eosinopénie.

Dans ce dernier groupe chez la majorité des malades on a pu observer à l'aide de l'ophtalmoscope des altérations profondes comportant une baisse remarquable de l'acuité visuelle et un scotome central très étendu. Mais dans bien des cas les altérations du fond de l'oeil étaient minimes, le scotome central peu réduit (5°) ou bien on n'a pu observer qu'un scotome relatif de couleur bleue, l'acuité visuelle peu réduite (5(10–5)25), le nombre des cellules eosinophiles n'a cependant point montré d'altération sous l'effet de la lumière (2). Cette observation est d'autant plus remarquable que dans les cas d'inflammation rétrobulbaire du nerf optique même à un scotome central absolu et très étendu et à une baisse remarquable de la vision ([illegible] M à la lecture au doigt) le processus n'a pas empêché non plus l'apparition normale de l'eosinopénie causée par la lumière (3).

Selon nos examens nous pouvons donc considérer comme point de départ de la fonction optique végétative une partie centrale peu

étendue mais bien decrite de la *retine*. La *voie optique se comporte* autrement que celle qui est purement optique, c'est pourquoi la voie optique et la voie opticovegetative doivent être separees l'une de l'autre non pas tant au point de vue anatomique mais plutot au point de vue fonctionnel.

L'examen de l'eosinopenie, causee par la lumiere, peut egalement fournir des resultats utiles dans la pratique ophtalmologique. En cas d'opacite de la *cornee lorsque l'emploi* de l'ophtalmoscopie est inexecutable on peut constater de telle *façon quel est l'etat du centre* de la retine, vaut il la peine de soumettre le malade age a une operation, par ex. peut on s'attendre a une bonne acuite visuelle a la suite de l'operation de la cataracte. Une cataracte bien developpee mais en presence d'une retine intacte provoque en effet une reaction d'éosinopenie, tandis qu'elle est eliminee en cas d'une dégeneration de la *retine qui se dissimule derriere la cataracte*.

L'examen de l'eosinopenie dans la *periode initiale* d'une *maladie* peut servir a *confirmer le* diagnostic. Dans un de *nos* cas l'examen d'un homme relativement jeune a revele une alteration du fond de l'oeil a peine appreciable, un scotome central tres reduit et une baisse relative de la vision. Le soupçon de l'aggravation a ete dissipe par ce fait que l'eosinopenie n'a pas eu lieu sous l'action de la lumiere.

Parmi les amblyopes de l'enfance il y a un groupe special de tels cas ou la cause des amblyopes se trouve dans la retine. *Il ne vaut pas la peine de* les exposer a des *traitements epuisants* et *superflus*. Leur isolement est possible par ce fait que nous ne provoquons pas de reaction d'eosinopenie sous l'action de la lumiere (4).

En ophtalmologie le nombre de tels examens est relativement reduit qui s'appuient sur le jugement objectiv du malade. L'introduction de l'examen de l'eosinopenie en diagnostic pourrait signifier un tel procede objectif.

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ARTERIOSCLEROTIC RETINAL VASCULAR CHANGES WITH AGING PROCESS IN HYPERTENSION

TETSUO IIZUKA

Jikei University, School of Medicine, *Tokyo, Japan*

(Director Prof K OHASHI)

I have studied on the changes of ocular fundus in hypertensive patients and have already reported the scoring method to evaluate the degrees of arteriosclerosis in retinal vessels

I concluded in my previous Japan report that the crossing signs were most important to diagnose the hypertensive ocular fundus in adult

But in older persons their fundus changes were very different from that of adult and sometimes it seemed difficult to determine the diagnosis of arteriosclerosis due to aging process on the retinal vessels

Therefore I wanted to find a rule to diagnose and classify the arteriosclerotic fundus changes throughout every generation and conducting a research at this time on every vascular change in hypertensive patients

As a first step of my study the following results of the examination ages from 20 to 70 patients totalling 340 patients

I measured their systemic blood pressure, retinal blood pressure and checked every changes in ocular fundus vessels such as vascular reflex narrowing of vascular lumen irregularity of vessel calibres opacities of vessel walls Gunn's phenomena and crossing signs Also I took a fundus photograph for recording

The results are as follows

(1) Vascular reflex (Table 1)

Table 1 shows a rate of vascular reflex in each generation

(−) Normal vascular reflex most frequently in 20 and 30 lesser in older generation and least in 60 But in 70 slightly increased

(±) Gradually decreased cases from 20 to 70

(+) Slight decrease in 40 slight increase in 50 and 60 In 70 decrease again

(++) Gradual increase from 20 to 70

(2) Narrowing of vascular lumen (Table 2)

Table 2 shows a degree and rate of the narrowing

(−) Normal vessel lumens highest in 20 After that, gradually decreased until 70

etendue mais bien decrite de la retine La voie optique se comporte autrement que celle qui est purement optique, c'est pourquoi la voie optique et la voie opticovegetative doivent etre separees l'une de l'autre non pas tant au point de vue anatomique mais plutot au point de vue fonctionnel

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Table 1

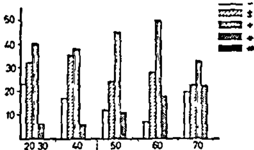


Table 2

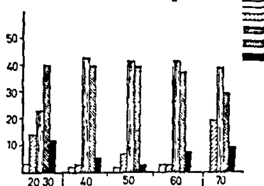


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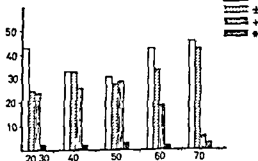


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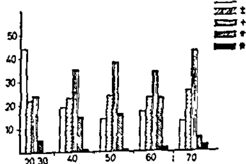


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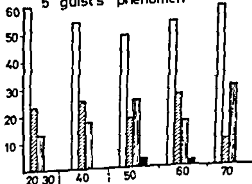
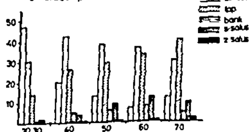


Table 6



(±) Highest occurrence at 40 after that almost no changes until 60
In 70 rapid increase
(+) In 20 lowest, in 40 rapid increase, after that, until 70 no changes
(++) In 20 and 40 highest occurrence, after that gradual slight decrease until 70
(3) Irregularity of vessel calibres (Table 3)
(−) Normal calibre, in 20 irregularity highest occurrence in 40 and 50 decreased in 60 and 70 increased again
(±) In 20 and 40 slightly increased, in 50 decreased
After that in 60 and 70 increased again
(+) From 20 to 50 increased but in 60 and 70 decreased
(++) No changes between each generation
(4) Opacities of vessel walls (Table 4)
(−) Vascular walls without any opacities highest at 20 until 50 rapidly decreased but no changes in 60 and 70
(±) From 20 to 70 slightly increased
(+) Until 50 relatively rapid increase in 60 same as in 50 in 70 increase again
(++) Until 60 slowly increased in 70 slightly decreased
(+++) From 20 to 70 gradually increased
(5) Guist s phenomena (Table 5)
Table 5 shows a rate and degree of Guist s phenomena in retinal vessels
(−) Negative Guist s phenomena most frequently seen in 20 until 50 gradually decreased after that slightly increased
(±) In 20 and 40 increased
in 50 decreased
in 60 increased again
in 70 decreased again
(+) Until 50 increased,
in 60 decreased
in 70 increased again
(++) No changes between 20 to 40,
in 50 rapid increase,
in 60 decreased
in 70 same as in 60
(6) Crossing signs (Table 6)
Table 6 shows a frequency of crossing signs in each type
(−) Negative pathological crossing signs
highest in 20 until 60 rapid decrease
but in 70 same as in 60

(i) Concealment
From 20 to 40, rapid increase,
after that gradual decrease until 70

(ii) Tapering
From 20 to 70 slightly increased

(iii) Banking
From 20 to 60, increased,
in 70 slightly decreased

(iv) S Salus
Almost same as Banking

(v) Z Salus
Found at 40 in the first, after that
in 50 slightly increased,
in 60 and 70, same as in 50

From these results, a difference could not be discovered of each generation Therefore, I executed a scoring method on all patients and discovered the following

According to the degree separations were made from 1–4 (Table 7)

Total score of each patient would mean the degree of arterios *clerosis*

Results were as follows (Table 8)

(1) Score of crossing signs
in 20 showing lowest score,
in 50 highest score,
in 70 lower than that of 50

Table 7

7 scoring

	scoring	1	2	3	4
	art reflex	±	+	++	+++
	calb narrow	±	+	++	+++
	calb irreg	±	+	++	+++
	wall opacit	±	+	++	
	guist phen	±	+	++	+++
cross phen	conceal	o			
cross phen	arch	o			
cross phen	tap		o		
cross phen	bank			o	
cross phen	s salus	o			
cross phen	z salus		o		

Table 8

8 average score of vascular changes

age	cross signs	vascul signs	total signs
20-30	10	49	59
40	18	69	87
50	26	74	100
60	25	72	97
70	20	73	93

(2) Score of other signs except crossing signs
in 20 showing lowest score,
in 50 highest one,
in 60 and 70 almost same as in 50

(3) Total score of all signs
in 20 lowest
in 50 highest,
in 60 and 70 almost same as in 50

From these results the crossing signs should be very valuable for diagnosis of hypertensive fundus changes in younger patients under 60 years of age as previously reported

But in older patients especially over 70 years of age that is not so valuable as in younger age Depending only on crossing signs evaluation at times be erroneous

I would like to stress from my research that we must emphasize for diagnosis of hypertensive fundus changes not only by crossing signs but also by other changes of retinal vessels

For this purpose my scoring method would be the most useful guidance to evaluate the fundus hypertension

(i) Concealment
From 20 to 10, rapid increase,
after that gradual decrease until 70

(ii) Tapering
From 20 to 70 slightly increased

(iii) Banking
From 20 to 60, increased,
in 70 slightly decreased

(iv) S Salus
Almost same as Banking

(v) *Z* Salus
Found at 40 in the first, after that
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cross phen	conceal	o			
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	tap		o		
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70 over	20	73	93

Yet contrary to such an anatomical and structural uniformity relating to the eye and its parts, no less impressive information presents a quite dissentient behaviour of the vasculous formations which occur in the vitreo retinal block which in opposition to the persistent uniformity manifested by all other parts display in that space an utmost variability

From what has been stated above one must fairly easily reach the conclusion that the actual subject in dispute of the matter under consideration does factually consist not only in reasons that, on the one hand call for such a firmly retained uniformity of the greater part of the eye through the entire differentiation of these animals and on the other claim for such an impressive and peculiar variability of the circulatory system in the vitreo retinal space represented by the vasculous formations as exactly are the hyaloid circulation in fishes and amphibians the conus vasculosus (papillaris) in reptilians, the pecten in avians and the direct vascularization of the retina in mammalians but also in reasons which call for such a tenacious retention of an inverted constitution of the retina of their eye

It stands to reason that the anatomical and histological uniformity of the eye and its parts rests upon biooptical grounds *in connection* with the functioning of this organ which physically *conceived prove* to be in their essentials very close in all classes of these *animals On* the contrary, the opposite phenomenon, the one of the *extraordinary* variability which occurs in the optical *space sensu strictiori'* cannot be of such a kind in nature for the reason *that even the* mere presence of a circulatory system in that *portion of the eye presents* a non transparent obstacle that impinges with *the course* of the light rays towards *photoreceptors i e* with the appropriate agent *of* this organ toward its actual goal and so *absolutely interferes* with its functioning

In line with this it is also an obvious fact that the other of the considered *phenomena* the inverted *constitution* of the retina represents less favourable *a state as regards* its functioning than does in fact afford its *opposite* for the simple reason that through such a state the quantity *of light energy* before having reached the photoreceptors is *reduced a good deal* by absorption of the retinal troma and actually interferes with the functioning of this organ

Here it is therefore pertinent *to state that* it was possible to reach further conclusions of *a predominant* importance as a result of a subsequent analytical work on this subject

Firstly that the actual shape and location of the vasculous formations in the *vitreo retinal space* are eminently dependent on the mode of subsistence that a *definite* group of these *organisms is* managing

Secondly that the inverted constitution of the retina is proved to be a result of an activity that takes place *on its surfaces*

MATHEMATICAL CONCEPTION OF THE DYNAMICAL PHENOMENON IN RESPONSE TO WHICH THE RETINA ASSUMED AN INVERTED CONSTITUTION

MLADEN SEBASTIAN, M D (*Zagreb, Jugoslavia*)

The problem in question arose from the study of the physiological meaning of some apparent but rather peculiar morphological phenomena which occur in the organ of sight in living organisms the body of which is supported by a vertebral column

In that respect, the present discussion is an outgrowth of studies on morphology of the eye in vertebrata given by the author in a monograph published in 1960 *

Its aim is to cover the morphological data with mathematically conceived physiokinetic instruments

The subject, we should like to start with, constitutes two most *important, though familiar, statements established on an almost* superficial approach to the matter involved

The one that states that the uniformity of this organ does truly *figure as one of the most impressive phenomena* throughout all classes of these organisms, irrespective of the mode of activity that they live, i e, from their lowest *still* living aquatic forms as exemplified by cylostomas, up to Man, the highest living organism endowed with a back skeleton

The second that says *that all representatives of this* large and prominent group of living organisms, in contrast to all others, proved to possess an inverted constitution of their retina

The first of these *statements does not* really refer only to the form of that organ and the parts of it, but is just so strictly true of its general anatomical make up, *the spatial interrelations* and the structures of its parts

In this respect, it should be emphasized that the uniformity of the eye *in vertebrata does not* only by *far surpass* the one of all the other parts of their body whenever such a phenomenon can be observed but that it does even *overtop the plainly conspicuous* uniformity manifested by the back skeleton, in accordance with which that group of organisms has been denominated

(*) Mladen Sebastian THE PROBLEM OF INVERSITY OF THE RETINA IN MAN AND THE ASSOCIATED PROBLEMS
Znanstvena knjizara Jugoslavenske Akademije ZAGREB YUGOSLAVIA

Yet, contrary to such an anatomical and structural uniformity relating to the eye and its parts no less impressive information presents a quite dissentient behaviour of the vasculous formations which occur in the vitreo-retinal block which in opposition to the persistent uniformity manifested by all other parts display in that space an utmost variability

From what has been stated above one must fairly easily reach the conclusion that the actual subject in dispute of the matter under consideration does factually consist not only in reasons that on the one hand call for such a firmly retained uniformity of the greater part of the eye through the entire differentiation of these animals and on the other claim for such an impressive and peculiar variability of the circulatory system in the vitreo retinal space, represented by the vasculous formations as exactly are the hyaloid circulation in fishes and amphibians the conus vasculosus (papillaris) in reptilians, the pecten in avians and the direct vascularization of the retina in mammalians but also in reasons which call for such a tenacious retention of an inverted constitution of the retina of their eye

It stands to reason that the anatomical and histological uniformity of the eye and its parts rests upon biooptical grounds in connection with the functioning of this organ which physically conceived prove to be in their essentials very close in all classes of these animals On the contrary the opposite phenomenon the one of the extraordinary variability which occurs in the optical space *sensu strictiori* , cannot be of such a kind in nature for the reason that even the mere presence of a circulatory system in that portion of the eye presents a non transparent obstacle that impinges with the course of the light rays towards photoreceptors i e with the appropriate agent of this organ toward its actual goal and so absolutely interferes with its functioning

In line with this it is also an obvious fact that the other of the considered phenomena the inverted constitution of the retina, represents less favourable a state as regards its functioning than does in fact afford its opposite for the simple reason that through such a state the quantity of light energy before having reached the photoreceptors is reduced a good deal by absorption of the retinal stroma and actually interferes with the functioning of this organ

Here it is therefore pertinent to state that it was possible to reach further conclusions of a *predominant importance* as a result of a subsequent analytical work on this subject

Firstly, that the actual shape and location of the vasculous formations in the vitreo-retinal space are eminently dependent on the mode of subsistence that a definite group of these organisms is managing

Secondly, that the inverted constitution of the retina is proved to be a result of an activity that takes place on its surfaces

Furthermore, conclusive evidence has been provided that the phenomena being in point in either instance become produced by *one* and the same factor proved to be in the aquatic life the *mode of* motion and in the aerial one the activity *of the heart*

That is to say that the listed phenomena become *produced in* the first instance by *undulating movements of* the body, and in the second, the pulse of haemodynamics, and that there actually exists a reciprocal relationship between the motion in the aquatic life and *the haemodynamics* in *the* aerial one in the range of biophysics

In view of these facts it is of no neglectable *importance to state* here that this factor in either mode of life from the standpoint of biomechanics can easily be resolved into two components

In the pressoric one, which is produced in the aquatic life hydrodynamically on the external surfaces of the eye, and in the aerial one, haemodynamically inside the *vitreo retinal block*

Speaking in terms of mathematics, its ratio is given in the first instance, by the equation of Bernoulli, and in the second, by the extent of the amplitude of the pulse of the blood pressure inside that block, which means the space encompassed by Bruch's membrane

The other component, being a consequence of the principle of inertia, is produced in the aquatic life by undulating deflections of the eye masses to right and left from the direction of advance, and in the aerial one, by displacements of the eye masses through the pulsation of the lumen of the arteries

Mathematically expressed, the ratio of these components is given in either instance by the greatness of the impulse, i e the product of velocity multiplied by mass

Physically conceived, either component, being responsible for the listed phenomena, represents forces brought about in the first instance by the strain of the substance that the vitreo retinal block is built of, and in the second, by making active the masses of this portion of the eye

Of a particular interest is the fact that the very nature of these forces is such as to give no rise to effects of whatsoever physiokinetic activity as long as they occur in a homogeneous or, physically expressed, a continuous and isotropic medium But the vitreo retinal block presents a continuous and isotropic medium only up to the limit between the vitreous humour and the stroma of the retina or, speaking in words of physico chemistry, up to the interface between both portions of this block

Consequently, in that interface does exactly occur not only a mechanical discontinuance of the vitreo retinal block, but there also occurs a contact between two substances with plainly different physical properties

On the basis of these analytical remarks and data one is authorized to state here that it is a well established fact that a disturbance of any

kind in our case the first component of the factor represented by the compressional wave propagating in one medium and impinging upon an interface gives rise not only in general to reflected and refracted waves but also to a series of subsequent physiokinetic effects because of an interfacial sliding and friction between surfaces of the both fairly liquid but living substances being here in contact as well as to dissipation of heat, according to the first fundamental law of thermodynamics due to friction in that place and the second fundamental law of thermodynamics due to the transformation of the impulse that occurs in that place

It is further true that the second component of this factor, the activity of the masses made active by motion according to the principle of inertia engenders in the interface, representing a mechanical discontinuance, successive effects in response to different modes of vibration they become involved in en bloc', owing to different physical properties possessed by either portion of the vitreo-retinal block being in contact

The physiokinetic effects of the second component are found to be the same in nature as the ones of the first component but far more expressed

Speaking in terms of mathematics they represent periodic but unharmonic vibration the ratio of which is covered by the Fourier s theorem

Here it is therefore proper to state that from the standpoint of physiokinetics either component engenders effects on the retinal surfaces which substantialize inadequate influences to the retinal tissue but the more so to its specific sensory cell elements and which are proved to be disturbing and harmful to the functioning of the eye

From the discussion which has been given above it must be evident firstly, that the inverted constitution of the retina substantializes a protective disposition in particular for the photoreceptors because these extremely sensitive cell elements become by inversion merged in the mechanical homogeneity of the chorioretina, and secondly that the vasculous formations in the vitreo-retinal block with their shape and location substantialize special self protecting forms of the circulatory system well matched with the mechanical influences that their haemodynamics in a given case is involved in

RETINOBLASTOMA IN THE ADULT REVIEW OF LITERATURE AND REPORT OF CASE ASSOCIATED WITH A BENIGN MELANOMA

JOHN R FINLAY, M D
HERVE BYRON, M D

To date only four retinoblastomas in the adult have been reported in the ophthalmic literature The rarity of such a tumor warrants the presentation of any new case This is the first of a retinoblastoma in a senile patient in which, simultaneously, there is a melanoma

The documentation of primary neuroepiblastic tumors has long been confused by the dispute in terminology In 1864 v Graefe thought that the tumor represented a sarcomatous hyperplasia of the retina Two years later Virchow postulated that these tumors arose from glial cells of the retina and were therefore comparable to gliomata of the brain Flexner suggested the term neuroepithelioma in 1891 because of the presence of rosettes of epithelial cells Six years later, Wintersteiner adopted this term although it was not universally accepted In 1918 Fisher proposed the term neuroblastoma in view of the embryonic character of the growth Verhoeff suggested the name of retinoblastoma in 1924 for those malignant tumors originating from the neural cells of the retina He advocated reserving the name glioma for only those tumors which were true astrocytomas, e g derived from the supporting structure of the retina and NOT from the neural elements The name was officially adopted by the American Ophthalmological Society in 1926 Bailey and Cushing in the same year formulated a new classification for brain tumors into three cells based on the differentiation of the medullary epithelium lining the neural tube

1	Neuroblast	Neuronal cells
2	Spongioblast	mostly astrocytes ependymal cells
3	Medulloblast	glial cells neuronal cells

This served as a basis for Duke Elder's classification which considered the retinoblastoma as one of five types of primary neuroepiblastic tumors

1 RETINOBLASTOMA — malignant tumor arising in early youth, usually from the posterior part of the retina, composed of primitive cells, retinoblast, which are analogous to the medulloblast of the central nervous system These cells are small, closely packed, round or polygonal with large darkly staining nuclei and scant cytoplasm and appear extremely undifferentiated or anaplastic

2 NEUROEPITHELIOMA — malignant tumor arising from the external or internal nuclear layer of the retina, composed of primitive spongioblasts which are the same cells in the central nervous system and which manifest rosette formation This rosette formation rarely predominates in the overall histology of this tumor They are thought to indicate a somewhat slower growing and therefore less malignant neoplasm than the retinoblastoma The cytology in this tumor is more differentiated than the retinoblastoma

3 MEDULLOEPITHELIOMA — malignant tumor arising from the ciliary epithelium in the eye which in turn develops from the primitive retinal epithelium of the medullary epithelium of the neural tube of the brain These tumors are very rare In the infant it is manifest as a diktyoma In the adult it may develop from malignant degeneration of pigment epithelium

4 NEUROBLASTOMA OR NEUROCYTOMA — these tumors stem from neuroblasts and are characterized by a high degree of differentiation

5 ASTROCYTOMA — is a tumor arising from true glial tissue It is the most common brain tumor, but is very rare in the eye

The term retinoblastoma as recognized by American ophthalmologists includes both the neuroepithelioma and retinoblastoma of Duke Elder s classification

Verhoeff postulated that two distinctly different types of retinoblastomas exist The first type is congenital in origin or develops from some congenital anlage Tumors of this type rarely manifest themselves later in life The second type arises late in life from cells which were originally normal Our case report falls into the second category

Reese feels that the tumor arises from primitive retinal epithelium In his classic book on tumors of the eyes, he cites Parkhill and Benedict's belief that most of these tumors arise from the inner retinal layers Since glial cells predominate in this layer they use this as an argument that the most probable origin of retinal tumors is the dedifferentiation of these glial cells Reese vitiates this theory by noting the difficulty of trying to ascertain which specific layer of the retina the tumor originates

Report of Case

HISTORY

M D P white female age 74 years was first seen by Brittain F Payne M D on April 6 1955 complaining of acute pain in the right eye She stated that vision had been lost without pain six months earlier Examination revealed a hard globe corneal edema shallow anterior chamber and no light perception The fundus was not visible A diagnosis of absolute glaucoma was made but the presence of an intra-ocular tumor was discounted on the basis of a normal transillumination Bilateral nuclear cataracts were present Vision in the left eye was correctable to 20/50

GENERAL DESCRIPTION OF GLOBE

Horizontal sections of the prepared globe were of normal size and shape, measuring 24 × 24 mm (AP × horizontal) *The retina showed thickening and deep basophilic staining* and complete detachment by a sub retinal protein precipitate Posteriorly, the growth was limited by *the lamina cribrosa but in this area there was exten ion to the* adjacent choroid The iris showed loss of crypts and folds There was *a basophilic thickening centrally and peripherally* it showed broad peripheral anterior synechiae *The lens was sclerosed On the nasal side there was a fusiform pigmented tumor of the pars plana of the* ciliary body

MICROSCOPIC DESCRIPTION

CORNEA The cornea was not remarkable There *was no evident* microcystic edema Peripherally there was some vascular engorgement Posteriorly and temporally in the area of the pseudo angles *there* was a membrane of tumor cells which covered the endothelium

LIMBUS The epithelium was normal The sub epithelial tissue *showed some vascular engorgement and perivascular round* cell infiltration The stroma showed tumor infiltration into the collecting vessels The chamber angle was closed by PAS on both sides The pseudo angle was covered by a neoplastic membrane The trabecular meshwork was compressed and Schlemm's canal was *filled with cellular* debris, pigment and tumor cells

SCLERA *The sclera was not remarkable Nasally, 2 mm* from the limbus, there was a nerve loop of Axenfeld

LAMINA CRIBROSA The lamina cribrosa was of *normal contour* The tumor growth had not infiltrated posteriorly into the nerve

IRIS The iris was atrophic There was loss of the crypts and folds and posterior festoonations There were broad PAS Anteriorly there was a dense neoplastic *membrane which had produced an ectropion uvea* Small round cells had invaded the stroma in focal fashion anterior to *the sphincter muscle Elsewhere the stroma* was replaced with fibrous tissue

CILIARY BODY The ciliary body showed similar atrophy On the nasal side in the area of the pars plana there was a fusiform densely pigmented tumor 3 × 5 mm *in length Posteriorly* it involved the long ciliary nerve to the equator and anteriorly to 1 *mm from the nerve loop of Axenfeld* Depigmented sections showed the tumor composed of spindle cells densely filled with *melanin* pigment granules, long fusiform nuclei, abundant cytoplasm with tapered ends arranged in parallel bundles This growth represented a benign Schwannian melanoma

CHOROID The choroid was unremarkable There was slight atrophy and diffuse round cell infiltration The lamina vitrea was

apparently intact and had resisted the spread of the tumor into the choroid However, where it was absent about the optic disc the tumor had spread about the intermediate tissue of Kuhnt into the choroid largely on the nasal side for 1 mm

RETINA The retina was detached from the ora to the optic disc It was thickened most markedly posteriorly disorganized and almost entirely replaced by neoplastic cells These cells were seen to arise from the inner nuclear layer They showed a perivascular arrangement which had been termed pseudo rosettes The tumor had broken the internal limiting membrane posteriorly and had spread into the vitreous cavity Externally it had spread through the external limiting membrane and had diffusely spread into the sub retinal serous fluid It had penetrated beneath the pigment epithelium and had formed a dissecting membrane between Bruch s membrane and the pigment epithelium

The sub retinal space was filled with free floating tumor cells, red cells and macrophages The tumor was composed of large densely arranged round and polyhedral cells having large nuclei with well defined nucleolar walls They were rather pale with coarse clumping of the nuclear chromatin The cytoplasm was scarce and poorly staining, showing almost bare nuclei Mitotic figures were frequent There was no calcium present However areas of marked karolysis and pyknosis suggested early necrosis

ANTERIOR CHAMBER The anterior chamber was decreased in depth and diameter by peripheral anterior synechia It was filled with protein precipitate

LENS The lens capsule was intact The subcapsular epithelium was normal There was some liquefaction degeneration of the cortex The nucleus was sclerosed

OPTIC PAPILLA The optic papilla was replaced by tumor tissue which extended to the lamina cribrosa

OPTIC NERVE The optic nerve showed no tumor invasion in the sections studied

OPHTHALMOLOGY PATHOLOGY DIAGNOSIS

Retinoblastoma right eye
Glaucoma secondary
Benign Schwannian melanoma.
Retinal detachment solid
Tumor invasion of choroid
Tumor implantation on iris

CLINICAL COURSE

The slides were reviewed by many outstanding ophthalmic pathologists April, 1956, who concurred with the diagnosis

Dr Verhoeff commented at the time that with such typical spread of the retinoblastoma to the choroid he had not seen a case survive more than a year

May 12, 1956 The patient was admitted to Jacobi Hospital with right hemiplegia and motor spasm of four weeks duration Craniotomy was performed for intra cranial space taking lesion Biopsy of a frontoparietal lesion was taken The patient died July 27, 1956, and autopsy was performed at Jacobi Hospital

SUMMARY OF AUTOPSY FINDINGS

BRAIN "The tumor occupying the left frontoparietal region measured about 10 cm in diameter which was adherent to the dura There was no evidence of herniation The right optic nerve was smaller than the left Sections of the adjacent areas, basal ganglia, and cerebellum showed many foci of perivascular infiltrates

The meninges over the main lesion showed slight to moderate degree of monocytic infiltration with some lymphocytes

Primary 1 Tumor, left frontoparietal lobe
2 Remote status — Post operative craniotomy

Secondary 1 Cholelithiasis
2 Chronic passive congestion and fatty infiltrate of liver
3 Right pleural adhesion
4 Remote enucleation, right eye

Microscopic sections taken from the central area of the tumor showed an infiltrating lesion composed of highly cellular elements The cells were round, oval or polygonal and uniform in size There was scant cytoplasm with almost naked nuclei The nuclei had prominent walls and coarse clumping of chromatin Mitotic figures were infrequent The cells were loosely arranged with little stroma The tumor was not highly vascular However, in the periphery there was perivascular infiltrates of cells The cells showed even distribution, were well preserved and no areas of necrosis or calcification were seen (Photo 10 × 11–12)

The cytologic identity of the retinal and cerebral tumor was unmistakable" (See Figures 9 and 11)

REVIEW OF LITERATURE

Verhoeff published the first American report of a retinoblastoma in an adult in 1929 In his paper he mentioned *Wintersteiner's* documentation in 1897 of 167 patients manifesting this tumor the oldest of which was sixteen years old He also cited Magby's report in 1919 of a patient who had a glioma retinae in her right eye at the age of two years When her left eye was enucleated at the age of twenty years

because of glaucoma, it was found to contain a large retinoblastoma This patient was the oldest to harbor this tumor before Verhoeff reported his case In his paper Verhoeff cited two case reports of Gerard and Detroy, and Gerard and Morel in which a sixty six year old female and thirty five year old male presumably manifested this tumor He doubted the validity of these reports because of their brief pathologic descriptions and lack of photomicrographs A summary of Verhoeff s case report is as follows

A forty eight year old white male was admitted to the Massachusetts Eye and Ear Infirmary because during an examination one week before he had noticed that the sight in his left eye was almost gone This was unaccompanied by pain but he did have a feeling of numbness on the left side of the head

Examination of his eyes revealed a normal right eye The only abnormalities noticed in the examination of his left eye were a moderate number of cells in the A C dilatation of the iris vessels poor reaction of the pupil to light posterior synechiae at 7 o clock posterior cortical cataract and a vitreous full of fine opacities There was a circumscribed separation of the retina on the nasal side anteriorly The projection was irregular in contour and its surface showed prominent blood vessels It trans illuminated fairly well but irregularly The tension was 24 mm The vision in his left eye was finger counting at two feet

The left eye was enucleated on the day of admission with a clinical diagnosis of intra ocular neoplasm The patient was seen seven months later at which time his general health was found to be excellent

The globe was of normal size and shape on macroscopic examination In the upper nasal quadrant there was a large, greyish white intraocular tumor which extended from the root of the iris to a point 3 mm from the optic disc and from the vertical meridian above to slightly below the horizontal meridian

Microscopic examination showed that the anterior portion of the growth was situated within and greatly distended the ciliary body, anterior choroid and suprachoroidal space The inner layers of the choroid and ciliary body and ciliary processes were relatively intact and formed a covering for the tumor There was however, a gap 3 5 mm wide beginning 8 mm from the filtration angle where the uvea had been broken through by the tumor which here attained its greatest thickness

The parenchyma of the tumor consisted almost exclusively of rosettes of various sizes identical in appearance with those of a retinoblastoma Bordering the lumen of each rosette was a membrane analogous to the external limiting membrane of the retina but the cells did not project through this membrane

Occasionally the appearance of a fairly long irregular tubule was produced entirely due to the compression of a large rosette

by the surrounding cells Rows of cells representing parts of walls of rosettes were often seen Many of these had obviously resulted from the invasion of rosettes by the neighboring cells Cells in mitosis were abundant throughout the tumor

The stroma of the tumor was scant There was no reticulum between the tumor cells Within the tumor there were numerous areas of necrosis Some of them were replaced by connective tissue Within the areas of necrosis there were frequently seen sharply defined circular areas of tumor cells, each area containing a central vessel These were really cylindric formations seen in cross sections, such as described and explained by Wintersteiner

Microscopic examination of the other parts of the eye showed nothing of special importance, aside from changes confirming the age of the patient Several beautiful photographs accompanied this article

The second authentic retinoblastoma in an adult was reported by McCrea in 1943 A summary of his case report is as follows

A 67 year old male was treated by an ophthalmologist for several years conservatively for cataracts of both eyes On March 1, 1937, an intracapsular extraction with complete iridectomy was performed on the right eye uneventfully At that time the left eye showed incipient cataract changes, fine vitreous floaters and a corrected visual acuity of 6/24 On February 26, 1942, his left eye revealed a cataractous lens with inaccurate light projection, a tension of 23 mm A week later a combined complete iridectomy and intracapsular extraction of the left eye was performed

A membrane was seen in the vitreous at that time The eye remained red and painful despite treatment of N A B, sodium salicylate and other procedures On April 29, a large hyphema appeared In view of the poor light projection and persistence of pain, it was advised to enucleate the globe

Microscopic examination revealed a normal cornea The anterior chamber contained a large hyphema Both iris and ciliary body were much atrophied Behind the iris there was an ellipse of compressed, amorphous material resembling lens material and surrounding this some loosely arranged vitreous containing blood Posterior to this was a completely detached and folded up retina Behind the retina and in relation to the choroid there was a good deal of albuminous exudate containing tumor cells At one point the origin of the growth from the external nuclear layer could be made out The choroid was invaded by cells at one place near the ora serrata The central part of the vitreous chamber (about 2/3 of the whole) was occupied by the growth It was a neuroepithelioma containing many rosette formations Much of the tumor was necrotic but a large part stained well The optic nerve was intact behind the lamina cribrosa but in front of this there was invasion of neuroepithelioma cells

This case was accompanied by an excellent picture unequivocally demonstrating rosette formations

In the same year Rasmussen reported a case occurring in a forty eight year old male The exact nature of this tumor was debatable as there was no photographic evidence and the report was rather nebulous as will be seen in the following summary

> A forty eight year old male with a negative past history presented himself in August, 1939 for treatment of keratitis In October 1940, he was treated again Treatment had to be reinstituted in November and December of the same year at which time he was hospitalized Examination at that time revealed a vision of light perception in his right eye and 6/6 in his left eye There was slight divergence strabismus The right eye presented ciliary injection with some shagreen of the corneal epithelium and a small macula at 5 o clock There were numerous KP s on the corneal epithelium Posterior synechiae and numerous coarse blood vessels in the iris were noted Details of the retina could not be determined although the reflex was red The tension in the right eye was 68 mm and was normal in the left eye as was the remainder of the examination The patient was treated with atropine sweating and milk injections A month after admission an iridectomy was done
>
> The tension remained unchanged Pilocarpine was attempted unsuccessfully The eye quieted down and the pain disappeared For the following two years he had recurrent episodes of redness and pain in this eye On November 22 1944, he was re admitted after several days of distress Examination at that time showed no light perception slight injection corneal shagreen and slight opacity with dense KP s The anterior chamber was flat and the iris was atrophic Enucleation was performed
>
> Macroscopically, a greyish red soft mass of tissue entirely filled the globe
>
> Microscopically a roundish tumor 16 × 14 mm, situated anteriorly in the eyeball involved all of the structures toward the lens The tumor was separated from the posterior part of the eyeball by a crescent shaped fissure which was an artefact because all around it there remained tumor tissue corresponding to the site of the retina
>
> The tumor consisted of large islets of preserved cell masses alternating with great masses of blood and a homogenous coagulate The tumor cells were preserved chiefly around the numerous vessels The tumor was built up of cells with round or oval, very strongly stained nuclei, here and there the tumor cells were arranged in not quite typical rosettes In most places they were very closely packed without structure
>
> Because of the rosettes this tumor was regarded as a neuroepithelioma but the small number of rosettes and the entire appearance

of the tumor classified it as less mature than the majority of neuroepitheliomas originating from the retina

O'Day reported the next valid retinoblastoma in an adult in a paper read at the Ophthalmological Society of Australia in Sydney on September 23, 1947

> A twenty nine year old male gave a history of loss of vision and pain in the eyeball after an injury Examination revealed a visual acuity of hand motion in the temporal field, elevated intra ocular tension and total hyphema Following a cyclodialysis, the pain and increased tension were relieved The patient returned one year later after another injury to the same eye with a completely blind and painful globe On examination at that time, the tension was again elevated, a large globe with a temporal ciliary staphyloma and total hyphema were found Enucleation was performed
>
> Opening of the globe revealed a tumor involving the retina, iris, ciliary body and anterior chamber Tumor cells were seen to be growing along a cyclitic membrane Microscopic study revealed an anaplastic area in the ciliary body, areas of cells surrounding blood vessels typical of retinoblastoma with numerous mitotic figures Actively growing areas alternated with necrotic ones No evidence of extra ocular extension could be found (There were no pictures or photomicrographs accompanying this report)

In the same year, 1947, Rychener reported the fourth case of a retinoblastoma in an adult as follows

> A thirty three year old female was referred to the author because she noted black spots before the right eye four days previously Her visual acuity corrected in both eyes was 6/7 5 The right eye was externally normal but ophthalmoscopy disclosed numerous thready and tad pole shaped vitreous opacities which did not cloud the fundus sufficiently to prevent recognition of an unusual cystic lesion below the optic disc which seemed superimposed upon an old chorioretinal scar with a superior crescentic boundary of black retinal pigment The lesion was a three lobed cystic affair, the upper lobe being slightly larger than the disc and about 1 diopter below it covered and invaded by many small vessels giving it a pinkish appearance in contrast to the smooth surfaced grey, translucent appearance of the two much larger lobes which were joined to it below Peripheral lesions of old disseminated chorioretinitis were observed Transillumination of the mass was normal except for the crescentic line of pigment marking the upper 2/3 of its boundary Intra ocular pressure was recorded as 13 mm in the right eye and 12 mm in the left eye, Schiotz Potassium iodide was prescribed
>
> One month later the patient's symptoms were relieved and her visual acuity was recorded as 6/6 She was not seen for the next three years at which time she stated that some dimness of vision

had appeared in the previous two months Her visual acuity was still recorded as 6/7 5 but the visual field disclosed a large superior temporal defect The cystic mass had now shrunken into one pedunculated irregular lesion the surface being rough and corrugated Transillumination was as before and intra ocular tension was normal On December 23 1943 the vision in the right eye was completely lost returned slightly for a month and then again diminished to light perception She now exhibited a complete retinal detachment with a crescentic tear up and out at 10 30 o clock Transillumination and intra ocular tension were still normal Enucleation was advised but refused by the patient

She returned five months later for a refraction of her left eye The right eye revealed a shallow chamber, a quadrangular pupil and an atrophic iris with newly formed vessels on its surface The rest of the examination was as before with the exception of an increased intra ocular tension to 50 mm, Schiotz Enucleation was performed on September 1 1944 and the eye was sent to the Army Institute of Pathology

Gross examination revealed a firm eye with a dilated pupil There were firm gelatinous exudates and a pale growth 6 5 by 7 mm beneath the detached retina The tumor was situated near the optic disc The iris and lens were dispatched forward

Microscopic examination showed a tumor arising in the retina adjacent to the nerve head composed of cells with scant cytoplasm and with round or nearly round nuclei of variable size Hyperchromatic nuclei and mitotic figures were abundant and in one area there were many large bizarre and multinucleated forms There was a marked tendency particularly near an area of choroidal invasion toward rosette formation Here pseudo and incomplete rosettes were seen Only two or three true Flexner Wintersteiner rosettes were found in over sixty sections There was one area of necrosis and around this, clumping of living cells about blood vessels was evident There were blood vessels and areas of hemorrhage around the tumor Tumor cells had seeded along the inner and outer retinal surfaces Adjacent to the tumor the retina had undergone gliosis fibrosis and calcification Beneath and peripheral to the tumor there were patchy lymphocytic infiltrations of the choroid with chorioretinal adhesions secondary pigmentation of the retina and obliterative changes in the retinal vessels

There were broad peripheral anterior synechiae a vascular membrane on the anterior surface of the iris and ectropion uveae The retina was extensively detached The lamina cribrosa was slightly depressed

In the discussion of the paper by Rychener Dr Georgiana Dvorak Theobald mentioned another adult retinoblastoma which had been brought to the laboratory of the Illinois Eye and Ear Infirmary

of the tumor classified it as less mature than the majority of neuroepitheliomas originating from the retina

O'Day reported the next valid retinoblastoma in an adult in a paper read at the Ophthalmological Society of Australia in Sydney on September 23, 1947

> A twenty nine year old male gave a history of loss of vision and pain in the eyeball after an injury Examination revealed a visual acuity of hand motion in the temporal field, elevated intra ocular tension and total hyphemia Following a cyclodialysis, the pain and increased tension were relieved The patient returned one year later after another injury to the same eye with a completely blind and painful globe On examination at that time, the tension was again elevated, a large globe with a temporal ciliary staphyloma and total hyphemia were found Enucleation was performed
>
> Opening of the globe revealed a tumor involving the retina, iris, ciliary body and anterior chamber Tumor cells were seen to be growing along a cyclitic membrane Microscopic study revealed an anaplastic area in the ciliary body, areas of cells surrounding blood vessels typical of retino blastoma with numerous mitotic figures Actively growing areas alternated with necrotic ones No evidence of extra ocular extension could be found (There were no pictures or photomicrographs accompanying this report)

In the same year, 1947, Rychener reported the fourth case of a retinoblastoma in an adult as follows

> A thirty three year old female was referred to the author because she noted black spots before the right eye four days previously Her visual acuity corrected in both eyes was 6/7 5 The right eye was externally normal but ophthalmoscopy disclosed numerous thready and tad pole shaped vitreous opacities which did not cloud the fundus sufficiently to prevent recognition of an unusual cystic lesion below the optic disc which seemed superimposed upon an old chorioretinal scar with a superior crescentic boundary of black retinal pigment The lesion was a three lobed cystic affair, the upper lobe being slightly larger than the disc and about 3 diopter below it, covered and invaded by many small vessels giving it a pinkish appearance in contrast to the smooth surfaced, grey, translucent appearance of the two much larger lobes which were joined to it below Peripheral lesions of old disseminated chorioretinitis were observed Transillumination of the mass was normal except for the crescentic line of pigment marking the upper 2/3 of its boundary Intra ocular pressure was recorded as 13 mm in the right eye and 12 mm in the left eye Schiotz Potassium iodide was prescribed
>
> One month later the patient s symptoms were relieved and her visual acuity was recorded as 6/6 She was not seen for the next three years at which time she stated that some dimness of vision

DATA CONCERNING THE VASCULAR ORIGIN OF THE DISK EXCAVATION

Prof PAUL WEINSTEIN, M D , D Sc
Budapest, Hungary

As to the development of the disk excavation, the literature records two different views namely the neurogenic and the vasogenic theories According to the neurogenic theory, the increased intraocular tension which deteriorates the disk by its causing a cavernous degeneration is an essential factor this fact is proved by the secondary glaucoma in which case it is certain that the excavation is being created by the pressure increase According to the vasogenic theory, an excavation could appear without any tension increase in consequence of the sclerosis of the blood vessels of the optic nerve due to the insufficient blood supply of the lamina cribrosa this circumstance is proved by the pseudo glaucoma The intraocular tension increase in the secondary glaucoma exerts a pressure according to Radnot, Goldmann etc to the blood vessels of the lamina cribrosa and the final effect is thereby even the vasogenic one

In our own experiments we have made examinations as regards the vasogenic theory of development of the pseudo glaucoma in connection with 13 cases including 9 women and 4 men patients (Table) The intraocular tension measured by Schiotz s tonometer was a normal one in all of these cases and neither a rise of the eye pressure nor an increase of the chamber angle resistance could have been observed as a result of the provocative tests

Radiological examinations of these 13 patients have proved a caroti sclerosis on the X Ray photograph of the cranium in 3 of these cases which is according to the earlier literature data (Knapp Thiel) a frequent appearance in case of the disk excavations without glaucoma In course of our further examinations we have dealt with fixing of the visual field by Flicker Fusion Frequency *method* In 8 cases out of 11 we were able to observe a concentrically constricted Flicker Fusion Frequency This phenomenon could possibly be referred to the statement of Francois according to which the extremely thin art centr nervi optici is actually the feeding vessel of the optic nerve the blood circulation could in this art centr n optici very easily become defective in case of a sclerosis of either the caroti or the art ophthalmica or the central artery of the optic nerve *itself* The development of a state of hypoxia can be observed in cases like that which can be expressed by the concentrically constricted FFF possibly in case of a complete field of vision observed by other methods In one of the cases we have been observing binasal hemianopia, while in another case an inferior

by Dr Leona Fordon This case was never formally reported in the literature, but will be summarized here

A sixty-six year old female came to her ophthalmologist with the complaint that she could not see to the left with her right eye, following a hit on her head by a window Examination revealed a large retinal detachment in the lower temporal region of that eye There was no pain A re attachment procedure was recommended and refused Two months later, the detachment became larger and had a peculiar greyish appearance and there was a slight decrease in light transillumination Enucleation was advised but refused until four months later at which time the eye had become painful At that time the eye had no light perception, and the tension was 60 mm Transillumination was negligible

Microscopic examination showed a white tumor with a 10 mm base on the choroid and a height of 14 mm

Microscopic section showed a typical neuroepithelioma, composed almost entirely of mature cells arranged in rosettes, most of which were round and many showed no connection with the retina and the base of the tumor invaded the choroid, suggesting that the tumor might be metastatic Serial section, however, showed origin to be the outer nuclear and the rod and cone layer of the retina The sides of the tumor were covered with a thick dense vascular connective tissue membrane, which probably encapsulated the tumor except at its origin, until its sudden expansion This fact suggested the possibility that the tumor may have been present in a quiescent stage for some time There were no areas of necrosis

SUMMARY

The brain metastasis caused the death of the patient This was the first such specimen found in which a benign melanoma had simultaneously grown

A case of retinoblastoma and simultaneous benign Schwannian melanoma in a senile patient was presented The typical cytologic and histologic features and characteristic clinical course with spread *to the choroid* about the disc seedlings *to the iris and eventual brain metastasis made the diagnosis* certain

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hemianopia Taking no consideration to the X Ray photograph of the skull and to the FFF, the scleral rigidity was below 0 0,17 (0 0,08–0 0 13) in 5 cases out of 8 and in 3 cases it was below 0 0 2 In this regard we have to mention the case of two elderly sisters whose value of rigidity was 0 0 08 and the case of a younger patient who was suffering of a one side pseudoglaucoma with a deep excavation and had a completely normal disk on the other side The scleral rigidity was 0 0, 24 on the sound eye, while on the eye with the excavated disk it was 0 0 13 This means that the congenitally low rigidity of the sclera could create a predisposition to a pseudoglaucomatous excavation

A rather peculiar phenomenon was the fact that in a certain part of the cases with decreased scleral rigidity we were able to observe smaller oscillations than the normal ones in the oscillogram taken from the upper arms of the patients which is a sign of a hypoplasious blood vessel system It also occurred that the oscillations were lower on the side of the eye with decreased rigidity than on the other side

Summarizing all the above mentioned data we are able to state that the disk excavation is a vasogenic process in pseudoglaucoma which develops in consequence of the sclerosis of the optic nerve s own blood vessels The FFF perimetric narrowing is an introduction of the vasogenic hypoxia The lower rigidity of the sclera is a prediposing factor

I take this opportunity to thank the National Council to Combat Blindness Inc who were kind enough to enable us to accomplish a part of these examinations

Table

Case No	Sex	Age	Blood pressure	Flicker	X ray	Oscillometry	Rigiditas /R/ Outflow coeff /c/
1	Female	78	180/100	Conc lowered		36	R 008 C 0 24
2		76		Binasal hemian			R 01
3		72	190/100	Conc lowered	caroti sclerosis		
4		70	150/100				
5		41	140/80				
6		46	110/70	Normal		40 l d 22 l s	R o d 02 R o s 013 C o u 0 25
7		33	100/70			16	R 017 C 0 20
8		42	140/9)	Normal			R 008 C 0 24
9		55	120/90	Conc lowered	caroti sclerosis	28	R 017 C 0 24
10	Male	70	130 80				
11		60		Hemianopia inferior			
12		46	120 80	Conc lowered		40	R 008 C 0 24
13		,7	100 70				R 017 C 0 22

1 and 2 cases are sisters

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A NEW METHOD OF CLINICAL STUDIES FOR OPTIC NERVE HYPEREMIA

YOZO SUZUKI

Jikei University School of Medicine, *Tokyo, Japan*

(Director Prof K OHASHI)

Pressure on the eyeballs produce functional changes in various organs of the body which are *under the control of the autonomic nervous system* This well known *phenomenon* is called Ashner's *phenomenon* *Together with* changes which occur in the entire body as a result of pressure on the eyeballs, it is expected that changes also occur in the eyeballs themselves

The accurate measurement of vessel caliber of the ocular fundus is of great importance in the diagnosis and determination of prognosis of diseases of the fundus *or* general diseases accompanied by changes in the ocular fundus So far there has been no simple clinical method of accurately describing changes in the ocular fundus when examined ophthalmoscopically, and the observer usually *has to depend on* his subjectivity *Especially, in ophthalmoscopic examination of diseases of the optic nerve*, diagnosis *become difficult when the change observed* is slight

Numerous report have already been published on functional *changes* in *various body organs* caused by *pressure on* the eyeballs, however, reports *on changes in the retinal vessel caliber* caused just after pressure on the eyeballs *are seldom seen*

This presentation deals with my attempt to establish a diagnosis method for diseases of the fundus by observing functional changes in the retinal *vessel caliber From these changes* the condition of disc hyperemia *may be known*, and *from which an indirect clinical* diagnosis of diseases of the optic nerve *may be made*

The author's method of measurement is as follows

The Jikei university method of caliber measurement was *further* improved by using a *Gullstrand's ophthalmoscope* and a screw micrometer The screw micrometer is divided into three parts the ocular, the gauge and the objective As shown in fig 1, the gauge is graduated and by turning the *handle* the cross in the centre may be *moved* After *manipulating so that the blood* vessel of the subject *to be examined* is at right angle to the horizontal line at the bottom *the cross is moved* to coincide with one wall of the *blood* vessel Next, the cross is moved to coincide with the other wall of the vessel The

reading of the distance which the cross moved is thus taken Since the micrometer revolves around the optical axis retinal blood vessels running in any direction may be measured

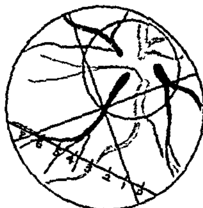


fig 1 retinal micrometry

PRELIMINARY EXPERIMENT

In this experiment the relation between the amount of pressure on the eyeball and the distension ratio of the vessels was studied By using a Bailliart s ophthalmodynamometer pressures of 10, 20, 30 50 and 100 gm were applied for varying intervals of 1 2 3 5 and 10 min As a result of this experiment it was determined that the most adequate pressure and duration of time of application were 50 gm and 3 min respectively

PROCEDURE OF THE MEASUREMENT

After sketching the disc and peripapillary retinal vessels with the aid of a hand ophthalmoscope measurements of the vessel caliber of the superior inferior temporal and nasal arteries and veins were made at the papillary margin by using the screw micrometer just described Measurement of the diameter of the disc was also made Next by means of Bailliart s ophthalmodynamometer a pressure of 50 gm was applied directly on the bulbar equator from the outer canthus for 3 min Directly just after release of pressure, measurements of the vessels just described were again taken However, the readings on the gauge cannot be taken as the true values of vessel caliber — they must be considered in relation to an object in the retina with a fixed dimension For this the ratio of the caliber of the retinal vessels to the diameter of the disc was computed according to Lobeck Also the percentage difference in the caliber of the retinal vessels before and after application of pressure was calculated

RESULTS

Aside from the 100 normal eyes used as experimental subjects, the following diseased eyes were also observed 10 papilledema, 5 simple optic atrophy, 5 inflammatory optic atrophy, 5 axial optic atrophy, 5 retinal optic atrophy, 5 papillitis and 50 retrobulbar optic neuritis These abnormal eyes showed typical fundus changes and their diagnosis had been confirmed by various other tests

Micrometric observations were made on the superior nasal artery (ASN), inferior nasal artery (AIN), superior temporal artery (AST), inferior temporal artery (AIT) superior nasal vein (VSN), inferior nasal vein (VIN), superior temporal vein (VST), and inferior temporal vein (VIT) Classification of distension ratio was done as shown in table 1 According to this classification those with lower than

TABLE 1 — *retinal vessel calibers and compression ratio of normal eyes*

	before compression	*after compression*	*compression ratio*
ASN	0 066 ± 0 0009	0 071 ± 0 0012	8 2 ± 0 64
AIN	0 066 ± 0 0014	0 071 ± 0 0015	7 9 ± 0 41
AST	0 077 ± 0 0016	0 086 ± 0 0016	14 8 ± 0 67
AIT	0 075 ± 0 0014	0 086 ± 0 0016	13 8 ± 0 64
VSN	0 086 ± 0 0018	0 097 ± 0 0020	12 2 ± 0 62
VIN	0 086 ± 0 0017	0 092 ± 0 0020	10 3 ± 0 29
VST	0 108 ± 0 0021	0 130 ± 0 0024	20 0 ± 0 90
VIT	0 109 ± 0 0022	0 130 ± 0 0028	18 5 ± 0 58

normal distension ratio, such as −I, −II, −III, have each a difference of five, but those with higher than normal distension ratio such as I, II, III, IV have each a difference of two Before this classification was made an attempt was made to classify with five each and also two each as the differences for both (−) and (−), however, with these the characteristic curves for each disease could not be obtained This being the case, it was thought that the mechanism of blood vessel distension differed between the (−) group and the (+) group and so after finding the maximum point of each the present classification was made

Table 1 shows retinal vessel caliber and distension ratio before and after application of pressure, of 100 normal eyes, excluding those with refraction error Table 2 shows difference of distension ratio

between arteries and vein of normal eyes Table 3 shows difference of temporal and nasal and table 4 shows difference of upper and lower

TABLE 2 — *difference of compression ratio between artery and vein of normal eyes*

	artery	*vein*	*difference*
SN	8 2 ± 0 64	12 2 ± 0 62	3 8 ± 0 89
IN	7 9 ± 0 47	10 3 ± 0 29	2 9 ± 0 54
ST	14 8 ± 0 67	20 0 ± 0 90	5 3 ± 1 11
IT	13 8 ± 0 64	18 5 ± 0 58	4 6 ± 0 86

TABLE 3 — *difference of compression ratio between nasal and temporal vessel of normal eyes*

	nasal	*temporal*	*difference*
As	8 2 ± 0 64	14 8 ± 0 67	6 6 ± 0 92
Ai	7 9 ± 0 41	13 8 ± 0 64	6 3 ± 0 76
Vs	12 2 ± 0 62	20 0 ± 0 90	7 8 ± 1 09
Vi	10 3 ± 0 28	18 5 ± 0 58	8 2 ± 0 65

TABLE 4 — *difference of compression ratio between upper and lower vessels of normal eyes*

	upper	*lower*	*difference*
AN	8 2 ± 0 64	7 9 ± 0 41	0 9 ± 0 18
AT	14 8 ± 0 67	13 8 ± 0 64	0 9 ± 0 03
VN	12 2 ± 0 62	10 3 ± 0 29	2 0 ± 0 68
VT	20 0 ± 0 90	18 5 ± 0 59	1 5 ± 0 17

Table 5 shows retinal vessel caliber and distension ratio before and after application of pressure of eyes with optic nerve atrophy Figs 2 3 4 5 represent this graphically Table 6 shows papilledema and fig 6 is a graphic representation of same Table 7 and fig 7 shows early stage of papilledema Table 8 and fig 8 shows congestion stage and table 9 and fig 9 shows maximum stage Table 10 and fig 10 shows papillitis and table 11 and fig 11 shows retrobulbar neuritis

RESULTS

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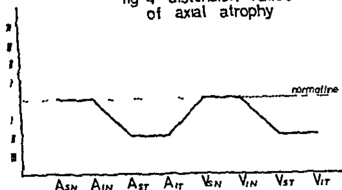


fig 4 distension ratios of axial atrophy

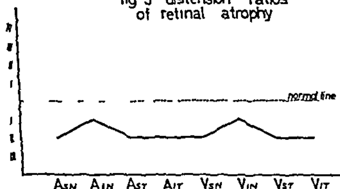


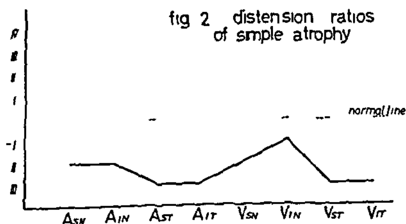
fig 5 distension ratios of retinal atrophy

TABLE 6 — *vessel calibers and compression ratio of chocked disc*

	calibers m.m before	after	ratio %
Asn	0 059	0 064	6 8
Ain	0 063	0 068	7 9
Ast	0 078	0 085	9 0
Ait	0 078	0 085	9 0
Vsn	0 102	0 121	18 6
Vin	0 102	0 121	18 6
Vst	0 145	0 182	25 5
Vit	0 149	0 187	25 5

TABLE 5 — *vessel calibers and compression ratio of optic nerve atrophy*

	simple atrophy			*inflammatory atrophy*			*axial atrophy*			*retinal atrophy*		
	bef	*aft*	*ratio*	*bef*	*aft*	*ratio*	*bef*	*aft*	*ratio*	*bef*	*aft*	*ratio*
ASN	0 043	0 043	0 0	0 048	0 048	0 0	0 065	0 071	9 2	0 051	0 051	0 0
AIN	0 043	0 043	0 0	0 066	0 067	1 5	0 066	0 071	7 5	0 050	0 051	2 0
AST	0 051	0 052	2 0	0 073	0 074	1 4	0 070	0 074	5 2	0 072	0 075	4 2
AIT	0 052	0 054	3 8	0 073	0 075	2 7	0 083	0 089	7 2	0 064	0 064	3 1
VSN	0 058	0 060	3 5	0 076	0 077	1 3	0 081	0 090	11 2	0 079	0 082	3 7
VIN	0 071	0 074	4 2	0 082	0 084	2 4	0 095	0 105	10 6	0 070	0 074	5 8
VST	0 086	0 091	5 8	0 111	0 114	2 7	0 117	0 131	10 6	0 100	0 109	9 0
VIT	0 083	0 088	6 0	0 101	0 106	4 9	0 116	0 132	12 1	0 100	0 108	8 0



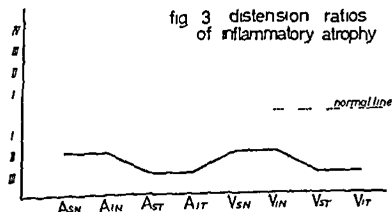
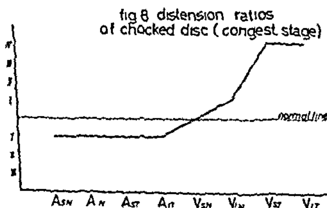


TABLE 8.—vessel calibers and compression ratio of chocked disc (congestion stage)

	calibers m m		ratio %
	before	after	
ASN	0 032	0 034	6 2
AIN	0 058	0 061	5 2
AST	0 070	0 077	10 0
AIT	0 070	0 076	8 6
VSN	0 067	0 075	12 0
VIN	0 096	0 108	12 5
VST	0 128	0 165	29 9
VIT	0 159	0 207	30 2

Further studies were made on the hyperemic grade of the disc and distension ratio of the retinal vessels of eyes with retrobulbar neuritis Those without disc hyperemia or with practically no change in the fundus but with subjective symptoms and central scotoma were referred to as 0 degree those with slight hyperemia of the disc, but



without other remarkable symptoms as II degree, and those with marked disc hyperemia indistinct disc margin and with irregular reflection in the maculopapillary area as III degree The curves described by each of these are shown in fig 12 13, 14

fig 6 distension ratios of chocked disc

TABLE 7 — *vessel calibers and compression ratio of chocked disc (early stage)*

	calibers m m *before*	*after*	*ratio %*
ASN	0 080	0 088	10 0
AIN	0 076	0 084	10 5
AST	0 100	0 114	14 0
AIT	0 096	0 107	11 5
VSN	0 096	0 112	16 7
VIN	0 136	0 160	17 6
VST	0 140	0 175	25 0
VIT	0 156	0 196	25 6

fig.7 distension ratios of chocked disc (early stage)

0–5 sec , and inflammatory atrophy in 8–10 sec Thus indicating that examination of the time of disappearance of redness may also be used as an aid to the early diagnosis of diseases of the disc

TABLE 10 — *vessel calibers and compression ratio of papillitis*

	calibers m m		ratio %
	before	*after*	
ASN	0 069	0 077	11 6
AIN	0 063	0 071	12 7
AST	0 076	0 093	17 0
AIT	0 082	0 095	15 9
VSN	0 100	0 118	18 0
VIN	0 104	0 121	16 4
VST	0 153	0 193	26 0
VIT	0 126	0 157	24 6

With my method it was found that in the normal eye the distension ratio of arteries was approximately 10 per cent and that of the veins above 15 per cent In simple atrophy and inflammatory atrophy,

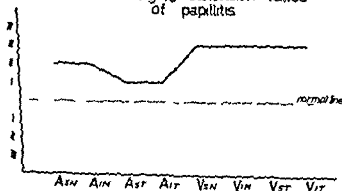


Fig 10 distension ratios of papillitis

the distension ratio of arteries was 0–4 per cent and that of the veins 2–6 per cent In retinal atrophy, the distension ratio of the arteries was 0–4 per cent and that of the veins 4–9 per cent, indicating that in these abnormal conditions the distension ratio is lowered In axial atrophy the distension ratios of both arteries and veins were normal

TABLE 9 — *vessel calibers and compression ratio of chocked disc (maximum stage)*

	calibers m m before	calibers m m after	ratio %
ASN	0 061	0 065	6 5
AIN	0 076	0 082	7 9
AST	0 099	0 112	13 1
AIT	0 084	0 094	11 9
VSN	0 099	0 119	20 2
VIN	0 107	0 136	27 5
VST	0 141	0 174	30 8
VIT	0 110	0 144	31 0

DISCUSSION

Forini in 1936 reported that while performing a fundus examination just after applying pressure on the eyeball redness was noted due to dilatation of the retinal vessels This redness, he stated, took more time to disappear in the eye with inflammatory disc than in the normal eye, whilst in the eye with atrophic disc hardly any redness was noted, or if present only very slight This he termed ophthalmo-angioscopia, and is being applied in the early diagnosis of inflammation

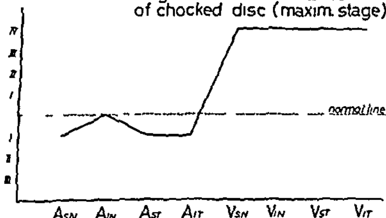
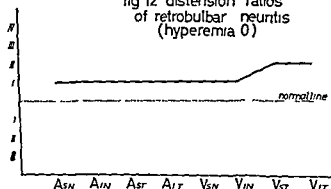
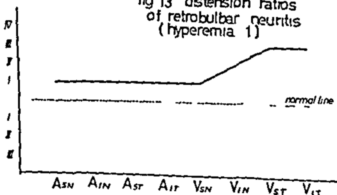


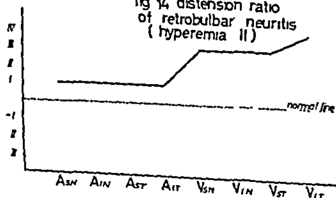
fig 9 distension ratios of chocked disc (maxim. stage)

or atrophy of the disc Prof Ohashi studied the time of disappearance of the redness and reported that the redness disappeared in the normal eye in 9–17 sec, in severe cases of simple atrophy and glaucoma in

I have here described a new functional examination method for observing change in retinal vessels and hope that it will be of aid in the diagnosis and determination of prognosis of fundus disease





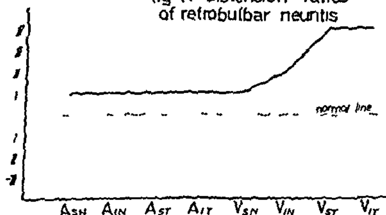


on the nasal side, whereas on the temporal side the distension ratio was markedly lowered

TABLE 11 — Vessel calibers and compression ratio of retrobulbar neuritis

	calibers m m		ratio %
	before	after	
ASN	0 059	0 065	10 2
AIN	0 063	0 070	11 1
AST	0 075	0 089	18 7
AIT	0 077	0 090	17 0
VSN	0 080	0 092	15 0
VIN	0 086	0 098	14 0
VST	0 111	0 140	26 0
VIT	0 117	0 147	25 8

In papilledema, the distension ratio of the arteries was 7–9 per cent, and nearly normal, whereas that of the veins was 19–26 per cent, and considerably high In papillitis, both the arteries and veins were considerably distended, especially the veins, but not so remarkable as in papilledema In retrobulbar neuritis as in papillitis, distension was



observed on both the nasal and temporal sides, however, in the arteries the differences on both sides were of the I degree and *only slight, but in the veins,* although on the nasal *side the difference* was of the I–II degree, on the temporal side, the difference was of the III degree

INTRA CRANIAL PART It is supplied mainly by a branch of the anterior superior hypophysical artery from the internal carotid artery No 'pre chiasmal artery' of Dawson (1948, 1958) was seen In addition minute collateral branches of variable number from the intra cranial and intra canalicular parts of the ophthalmic artery, which mostly run back to ramify on the pia, supply it The findings of Steele and Blunt (1956) agreed with those of mine Supply from the anterior cerebral and anterior communicating arteries has also been described by many authors (Wolff 1939, Magitot 1947, Francois et al, 1954 Hughes, 1958 and others)

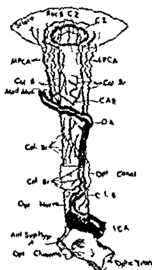


Fig 1 Sources of peripheral arterial supply to the various parts of the Optic Nerve as seen from above

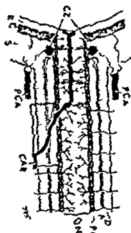


Fig 2 Schematic section of the Optic Nerve and Eyeball showing the pattern of arterial supply to the Intra-orbital and Intra-ocular parts of the nerve

INTRA CANALICULAR PART Small collateral branches from the intra canalicular and proximal intra-orbital parts of the ophthalmic artery supply this part with a rare contribution by twigs from other sources e g central retinal artery or other orbital branches of the ophthalmic artery These branches reach the nerve through fibrous tissue bands connecting the nerve with the surrounding dura a rupture of which during head injury may lead to haemorrhages and optic atrophy

INTRA ORBITAL PART It is supplied entirely by the ophthalmic artery

Posterior segment is supplied from the pial vessels which in turn come from the collateral arteries The collateral arteries usually one

THE BLOOD SUPPLY OF THE OPTIC NERVE AND ITS CLINICAL SIGNIFICANCE

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Since the time Haller (1754) and Zinn (1755) described an *arterial circle* in the sclera around the optic nerve, the subject of the blood supply of the optic nerve has been a centre of great controversy This is because attempts have been made to cover endless variations under single rigid description

The main controversial issues are

1 Origin, branches, distribution and anastomoses of the central retinal artery

2 Location, distribution and sources of the axial vascular system in the nerve

3 The central artery of the optic nerve

4 The blood supply of the lamina cribrosa and the intracranial part of the optic nerve

5 Anastomoses between the retinal and ciliary circulations

6 A logical interpretation of various clinical conditions in the light of vascular pattern

ARTERIAL SUPPLY OF THE OPTIC NERVE

For descriptive purposes, the optic nerve is divided into

(*i*) Intra cranial part

(*ii*) Intra canalicular part — lying in the optic canal

(*iii*) Intra orbital part, which can further be subdivided into two parts

- (*i*) Posterior segment — lying posterior to (*ii*)
- (*ii*) Anterior segment — in which the central retinal artery runs

(*iv*) Intra ocular part, which includes the regions of

- (*i*) Lamina cribrosa
- (*ii*) Optic disc

INTRA CRANIAL PART It is supplied mainly by a branch of the anterior superior hypophyseal artery from the internal carotid artery No 'pre chiasmal artery' of Dawson (1948, 1958) was seen In addition minute collateral branches of variable number from the intra cranial and intra canalicular parts of the ophthalmic artery, which, mostly run back to ramify on the pia, supply it The findings of Steele and Blunt (1956) agreed with those of mine Supply from the anterior cerebral and anterior communicating arteries has also been described by many authors (Wolff, 1939 Magitot, 1947, Francois et al 1954 Hughes 1958 and others)

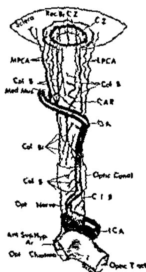


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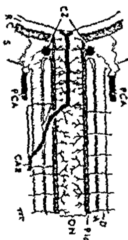


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INTRA CANALICULAR PART Small collateral branches from the intra canalicular and proximal intra orbital parts of the ophthalmic artery supply *this part* with a rare contribution by twigs from other sources e g, central retinal artery or other orbital branches of the ophthalmic artery These branches reach the nerve through fibrous tissue bands connecting the nerve with the surrounding dura a rupture of which during head injury may lead to haemorrhages and optic atrophy

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to three, rarely even more in number, arise usually directly from the ophthalmic artery and less commonly from the central retinal, medial muscular, medial posterior ciliary, *posterior ethmoid, supra orbital* or other muscular arteries These are located variably on the optic nerve but rarely on the lateral surface of the nerve

There is no axial centrifugal vascular system in the intra cranial, intra canalicular and the posterior segment of the intra orbital parts, except for a very rare small recurrent branch from the central retinal artery, which may run back in the centre of the optic nerve in the posterior segment for about 2–3 mm only

Anterior segment contains *peripheral centripetal vascular system,* as in the other parts, *formed by the pial vessels The pial vessels always* come from the central retinal artery, recurrent pial branches of the circle of Zinn and choroidal vessels, and the collateral branches of the ophthalmic artery *In the optic nerve, the distribution of these pial* branches from the central retinal artery is reverse of those from the collateral arteries of the ophthalmic, so that it seems one tries to cover up the gaps of the other, while the branches from the circle of Zinn and choroidal vessels are situated all round the nerve

In *addition an axial centrifugal system is seen in* this part of *the nerve in about 75%, which is always formed by the intra neural* br inches *of the central retinal* artery and not by the so called "artery of the optic nerve" *The* axial system supplies the centre of the nerve to a variable extent in this part of the nerve

Anastomoses All the pial vessels of the optic nerve anastomose freely with one another, particularly in the intra orbital part, before dipping into the nerve and run in its septa for a variable depth The anastomoses of the pial branches of the central retinal artery with (*a*) *those from the collateral* branches of the ophthalmic artery and (*b*) *the recurrent pial branches from* the circle of *Zinn* and the choroidal *arteries are free and prominent* Rarely anastomoses between the axial and peripheral *vascular systems are seen*

I want to stress here that the central artery of the optic nerve, as typically described by Behr (1935), Wolff (1939), Francois et al (1954, 1955, 1956), Wybar (1956) and others, was never seen by me This confirms the findings of Beauvieux and Ristitch (1924), Steele and Blunt (1956) and others If such an artery at all exists, it is extremely rare, as to be of no significance for all practical purposes Unfortunately *in the recent* past a lot of clinical importance has been attached to this artery

LAMINA CRIBROSA *It is mostly supplied by branches* from the circle of Zinn and also from the *choroidal vessels but no* branch from the central retinal *artery was seen by me in this part* So no anastomoses are seen between the ciliary and the *retinal arteries in* this region, though such *anastomoses at capillary level do* exist because of a continuity of the capillary *plexus of this region* with that of the optic disc anteriorly and *the adjoining part of the anterior segment*

of the optic nerve posteriorly In contrast to this well marked and free anastomoses between the pial branches of the central retinal artery and those of the circle of Zinn and the choroidal vessels are always seen as mentioned above

OPTIC DISC It is supplied by small branches from the central retinal artery and also gets branches from the adjoining choroidal vessels The capillaries of the disc are continuous with those of the lamina cribrosa posteriorly and the adjoining retina at the sides

The prominent and free anastomoses of the ophthalmic artery with the surrounding big branches from the external carotid artery e g middle meningeal, facial and infra orbital arteries and the arteries of the scalp can usually maintain the blood supply to the optic nerve and the eyeball efficiently in the event of blockage of the internal carotid artery

VENOUS DRAINAGE

The blood from the intra ocular and the anterior segment of the intra-orbital part is drained by the central retinal vein In the posterior segment for a variable distance a prominent tributary of the central retinal vein may be seen lying in the centre of the optic nerve In addition to these small veins corresponding to the small arteries are seen at places

VASCULAR DISORDERS OF THE OPTIC NERVE

I have included many clinical conditions *under this category*, on direct or indirect suggestive *evidence of vascular* interference Future researches and new evidence may relegate some of these to other categories of disorders

The disorders are classified as follows

I INFLAMMATORY DISORDERS

1 Temporal arteritis
2 Periarteritis nodosa
3 Thrombo angiitis obliterans
4 Ischaemic optic neuritis
5 Eales disease
6 Syphilitic optic atrophy

II DEGENERATIVE DISORDERS

1 Cavernous degeneration of the optic nerve
2 Cupping of the optic disc
3 Glaucoma and pseudoglaucoma
   (i) Vascular basis of pathological changes in the optic nerve
   (ii) Vascular basis of the field defects

(iii) Vasogenic basis for glaucoma and pseudoglaucoma
4 Arteriosclerotic optic atrophy

III THROMBOTIC AND/OR EMBOLIC DISORDERS

1 Occlusion of the central retinal artery
2 Occlusion of the central retinal vein
3 Occlusion of the ophthalmic artery
4 Internal carotid artery insufficiency

IV VASOMOTOR DISORDERS

Raynaud's disease

V TRAUMATIC DISORDERS

Optic nerve lesions in head injury

VI MISCELLANEOUS DISORDERS

1 Papilloedema
2 Optic nerve and retinal haemorrhages in intra cranial haemorrhages
3 Post haemorrhagic optic atrophy
4 Compression of the optic nerve
5 Marked oedema of the intra canalicular part of the optic nerve
6 Pulseless disease
7 Altitudinal hemianopias
8 Multiple sclerosis

In such a brief discourse, unfortunately, it is not possible to refer with any justification to any of these disorders However, it may be pointed out that, in many of these cases, it is not possible to interpret the clinical picture on the basis of the vascular pattern described above This is because of great discrepancy in our knowledge of aetiology, pathology and pathogenesis of most of the conditions Perhaps this long list of vascular disorders of the optic nerve may act as a stimulus for more intensive study of all these conditions

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ABBREVIATIONS USED

A	= Arachoid
Ant Sup Hyp Art	= Anterior Superior Hypophysial Artery
Br	= Branch
C	= Choroid
CAR	= Central retinal artery
CZ	= Circle of Zinn
Col Br	= Collateral Branch
D	= Dura
ICA	= Internal carotid artery
LPCA	= Lateral posterior ciliary artery
Med Mus	= Medial Muscular
MPCA	= Medial posterior ciliary artery
OA	= Ophthalmic artery
ON	= Optic nerve
PCA	= Posterior ciliary artery
R	= Retina
Rec Br CZ	= Recurrent pial branch of Circle of Zinn
S	= Sclera

LA TELEVISION RADIOLOGIQUE ET LE CINEMA SIMULTANE EN OPHTALMOLOGIE

par M NOIX (Paris) et L SARRAZIN (Nice)

La Television a deja penetré parmi les techniques d'exploration de l'oeil et nous rappelons a ce titre les essais de television du fond d'oeil

Mais, en retinoscopie, comme en endoscopie, les résultats, déja favorables, ne prendront toute leur valeur que lorsqu'il sera possible de realiser des tele transmissions en couleur Le noir et blanc ne procurant qu'une reproduction incomplete des contrastes

Il n'en est pas de meme en radiologie ou l'on ne recherche que des silhouettes La Television Radiologique permettra ainsi a l'Ophtalmologiste de developper avec son Collegue Radiologiste des contacts jusqu'alors assez limites

Si rien jusqu'a present ne peut remplacer le cliche radiographique classique, il faut reconnaitre les avantages que peut apporter à l'investigation ophtalmologique l'utilisation de l amplificateur de brillance Cet appareil ramene dans le domaine de la vision mesopique une image radioscopique jusqu'alors confinee dans le cadre restreint de la vision crépusculaire sans possibilite d'appreciation fine des details

Mais, en dehors d'une application directe de l amplificateur à l'examen du squelette orbitaire ou a la recherche d'un corps etranger profond, deux techniques nouvelles viennent etendre les perspectives experimentales et cliniques relevant de l'ophtalmologie

Il s agit d'une part du cinema radiologique dont le film constitue le document d'ordre dynamique et d'autre part de la Television Radiologique permettant l observation dans une salle eclairee avec des doses de RX tres faibles et un coefficient de securité exceptionnel pour le malade et l'observateur

Le cinema permet de reproduire les differentes phases d une exploration radiologique, *d'ou son double interet clinique et didactique*

La Television objective en milieu eclairé une image qui appartenait auparavant au domaine de l'obscurite ambiante et pour un seul observateur Le jumelage Amplificateur de Brillance chaine de Television en circuit fermé apporte a l'Ophtalmologiste un procéde d'examen dont nous allons degager les applications les plus elementaires, en attendant que l'experience et le temps en etendent le domaine

I. LES BUTS DU CINÉMA ET DE LA TÉLÉVISION RADIOLOGIQUE EN OPHTALMOLOGIE

Les buts auxquels nous avons pensé sont ceux dans lesquels un élément nouveau au diagnostic et au traitement peut être apporté par la notion du mouvement, c'est à dire l'exploration du squelette, la recherche et l'extraction contrôlées des corps étrangers du globe et de l'orbite, l'examen dynamique des voies lacrymales, de la motricité oculaire, du nystagmus, l'application à la neuro-chirurgie, l'angiographie cérébrale et l'étude de la circulation oculaire.

FIG. 1. — La télévision radiologique. Une caméra vidicon est jumelée avec un amplificateur de brillance radiologique. L'information après amplification peut être transmise à plusieurs téléviseurs.



(a) Téléradioscopie avec radiographie.



(b) Jumelage radiocinéma, téléradioscopie, radiographie.

1) L'examen du squelette avec l'amplificateur de brillance est une vision radioscopique permettant d'obtenir un centrage plus précis, plus judicieux du cliché avec une grande souplesse dans la découverte de l'*incidence optima*. L'observateur peut lui-même, à tout moment, sous le *contrôle de la vue*, mobiliser à la demande la tête du sujet et *préciser ainsi l'incidence* du trou optique ou de la fente sphénoïdale.

2) Le grand coefficient de sécurité permet la localisation exacte et l'extraction des corps étrangers *orbitaires* ou intra-oculaires, surtout lorsqu'il s'agit d'un corps étranger opaque non magnétique.

En effet, en vision crépusculaire, le pouvoir séparateur de l'oeil dépasse difficilement 3 à 4 m/m à la *brillance de l'écran* radioscopique

alors qu'il atteint 1 m/m en television radiologique et 5/10 de m/m en examen direct sur amplificateur

(3) Les voies lacrymales pourront etre explorees dynamiquement grace aux differentes phases du transit d'un liquide opaque aux RX Pendant qu'un aide pratique lentement l'injection, l observateur mobilisant la tete du malade, pourra decouvrir et localiser les stenoses et les diverticules Une indication therapeutique precise sera ainsi possible

(4) La motilite oculaire nous a paru devoir beneficier de ces techniques et nous vous apportons un exemple des mouvements conjugues des globes Le deplacement d index opaques solidaires des cornees par rapport a des reperes fixes judicieusement places permet d'objectiver la motilite normale et pathologique et d'envisager la presence exacte des deviation Une des applications principales sera l etude du *nystagmus*, en lumiere normale, dans l'obscurite et au cours du sommeil naturel ou artificiel Le film qui vous sera projeté vous montrera nos premiers essais ainsi que la persistance du nystagmus a l'obscurite et son attenuation apres l'occlusion des paupieres

(5) En neuro chirurgie les tumeurs intra ou parasellaires, a retentissement oculaire, devraient beneficier de l amplificateur de brillance La mise en place d elements radioactifs au voisinage de la tumeur, par voie endonasale, doit etre grandement facilitee A tous les instants la direction du trocart porteur des grains peut etre verifiee sur deux televiseurs donnant des vues orthogonales de chaque phase du catheterisme trans ethmoido sphenoidal

(6) En dehors de ces premieres applications d ordre clinique, la television radiologique et le cinema nous ont permis de reproduire dans un but experimental et didactique des angiographies cérébrales associees ou non a la ventriculographie Dans un exemple du au regrette Docteur Trotot, il s agissait d'objectiver un anevrysme de la cerébrale anterieure a retentissement oculaire

Dans le meme ordre d idee nous portons a l'attention du Physiologiste un essai tres imparfait d opacification des circuits vasculaires d'un oeil de bovide enuclee se terminant par celle du grand cercle capillaire de l'iris

Nous esperons ainsi, en demontrant les resources de l'amplificateur de brillance, provoquer des recherches dans le domaine de la physiologie et de la clinique oculaire

II MATERIEL ET TECHNIQUE D'APPLICATION

Le materiel que nous utilisons pour des premier essais nous est personnel Il est constitue par le jumelage d un amplificateur de brillance et de deux cameras, l une de cinematographie l autre de télevision, facilement substituables l une a l'autre grace a un systeme optique d une grande precision, mais dont la mise au point initiale presente certaines difficultes Ce systeme, permet de passer instantanement de l'examen télevise a la prise du film et par l adaptation d un

selecteur radiologique de prendre les cliches radiologiques au temps opportun

Cet ensemble est d un poids total inferieur a 20 Kg Il est fixe sur une colonne mobile qui en permet le deplacement dans les trois dimensions de l espace que le malade soit assis ou couche

Les images téleradioscopiques etant donnees dans une salle éclairee aucune adaptation à l'obscurite n est necessaire et toutes les manoeuvres chirurgicales peuvent etre effectuees avec le maximum de sécurite

Les cliches radiologiques, pris sous le controle de la vue, constituent les documents statiques indiscutables que le film pourra completer par des renseignements d ordre dynamique

Enfin, signalons que des essais satisfaisants ont ete faits sur l amplificateur de brillance dans le cadre de la reproduction stéréoradioscopique et du film en relief mais que la complexite du materiel laisse ces essais dans le domaine du laboratoire

III INTERPRETATION DES RESULTATS ET AVENIR DE LA METHODE

Nous avons choisi parmi nos documents ceux qui peuvent par une étude comparative montrer la valeur respective du cliche radiologique de l image de l amplificateur et de l image de l ecran de television

Mais le film que nous projetons par ailleurs au cours de ce Congres montrera par une succession ininterrompue d images, constituant autant de cliches radiologiques obtenues à la cadence de 8 16, 24, et meme davantage par seconde les differentes phases des examens ci dessus

L *avenir seul* grace à l interet que vous voudrez bien accorder à cette méthode permettra de faire un bilan exact des avantages *que* la Télevision et le cinema radiologiques auront apporte a l Ophtalmologie

Nous souhaitons que cet exposé se traduise par la meme etroite collaboration des deux disciplines radiologiques et ophtalmologique que celle qui a permis dans d *autres specialites* d eclairer certains points obscures de la Physiologie viscerale

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OPTIC GLIOMA

ARNOLD FORREST, M D (*U S A*)

Consideration of the problems presented by the glioma of the anterior visual pathways makes clear that there are many more questions than answers I shall present to you a study of 53 cases which may answer a few more of these questions

Since gliomatous changes may involve any part of the pathway — the nerve the chiasm the tract — the term optic glioma is a useful one because it includes tumor in any of these areas Among orbital tumors although optic glioma is uncommon, it is the seventh most frequent pathologic type[1] In the historical review it is of interest that as recently as 1940 Davis[9] found it necessary to emphasize that intradural orbital tumors may be of two common types There is today no longer any confusion between these two namely glioma and meningioma We shall be concerned only with the glioma Verhoeff[3] was among the first (1922) to describe the histology of the glioma He commented further that partial excision was adequate treatment — resulting in apparent clinical cure Because occasional recurrences have been noted following partial excision complete excision of the tumor is desirable A further definition of tumor is given below

CLINICAL FEATURES

A study of the literature shows that 90% of patients are less than 20 years of age the oldest being 60 years In our series 98% were less than 20 years of age and 80% were less than 10 years of age The youngest patient showed exophthalmos at birth and the oldest patient was 23 years of age

The previous medical and family histories are helpful only when a history of von Recklinghausen s disease is present

In our cases the most common single symptom was exophthalmos The proptosis was usually downwards only occasionally upwards or outwards It averaged 5 millimeters but was as much as 10 millimeters Tumor in the visual pathway lying only behind the optic foramen does not produce exophthalmos If the pathway is involved by glioma the presence of exophthalmos with rare exceptions is a necessary and sufficient sign for the diagnosis of glioma in the orbit Twenty three of 53 patients showed exophthalmos

The second most common presenting symptom was a visual defect Since so many patients with optic glioma are very young poor vision is often overlooked as a symptom and may be difficult to evaluate Sometimes the visual loss can be measured but in addition

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another hospital was treated by craniotomy when an intracranial mass was identified — then enucleation and excision were performed

Patients with visual defect due to optic glioma but without proptosis carry a much graver prognosis for the reason that the lesion is intracranial All of these 17 patients received radiation except two who died before it could be carried out One patient had a subsequent Kroenlein operation and is well 18 years later Two patients are well after 10 and 18 years respectively Only four have died Others have been followed less than 4 years

Patients with strabismus as the most conspicuous symptom present essentially the same problem as those with poor vision Of these 9 patients one was treated by Kroenlein excision and all others have been radiated Two have died one is well 10 years later and the others have been followed less than 2 years Of the patients with increased intracranial pressure 3 of 4 have died but one is well 14 years after radiation One patient with nystagmus is well 7 years after radiation

These data represent the relationships of several characteristic symptoms to the site of lesion and subsequent outcome following treatment How do they determine the management of an individual case?

DISCUSSION

Any neurologic or x ray evidence of intracranial involvement by optic glioma immediately places the problem in the hands of the neurosurgeon Included in the former would be perimetric signs of chiasmal, tract or bilateral nerve involvement Among the latter would be changes in the sella — V or pear shaped distortion — eroded clinoids dilated ventricles involvement of the third ventricle or hypothalmos

This however leaves unsolved the *meaning* of dilated optic foramen One is tempted to assume — res ipsa loquitur — that this bony change implies involvement of both orbit and cranial cavity and that exploration of both chambers is *mandatory*

However there does not exist a *significant* study of the tissue derived from both sides or within the canal in patients with optic glioma and radiologically enlarged foramina There is *on the other hand* statistical data which has been here presented that excision of the orbital tumor is adequate therapy *in many* cases Further pathologic material (Reese[4] Forrest[5]) has demonstrated that much of the tumefaction in this material is *not actual glioma* but is reaction of the arachnoid sheath surrounding the nerves or hyperplastic gliosis in the nerve adjacent to the *tumor* (Figure 1 Sections A and D) The sketch suggests the configuration of some optic gliomas Either of these changes could result in a dilated foramen but would not constitute tumor on both sides of the canal

Therefore *optic* glioma in the orbit without clinical evidence of intracranial disease — even in the presence of the characteristic dilated foramen should be treated by orbital exploration and excision

poor fixation and loss of pupillary reflex to light may be noted When bilateral, blindness is recognizable even in the very young However, in one patient the vision was 20/20 in each eye

Strabismus resulted, usually, from loss of vision Glioma is not an invasive tumor and ocular deviation does not result from involvement of motor nerve or muscle This contrasts with strabismus which occurs when infiltration results from meningioma or hemangioma Some patients with optic glioma showed symptoms related to increased intracranial pressure or nystagmus

Changes in the ocular fundi were common Of the 23 patients with exophthalmos, all unilateral, 18 showed one normal nerve On the affected side 15 showed papilledema and 3 showed primary optic atrophy Two patients had bilateral optic atrophy and in 3 instances there was no comment *In the patients without exophthalmos, unilateral optic* atrophy was common, a few patients showed bilateral optic atrophy and a few papilledema on one side and optic atrophy on the other

Patients with any of these signs and symptoms were studied by X ray examination of the skull, including measurements of the optic foramina Those with intracranial disease showed a variety of skull changes involving the sella and the third ventricle The optic foramina were normal in many of these patients although both optic foramina were dilated in some instances and exophthalmos was rarely present

Although there is a wide range of normal sizes, a foraminal diameter over 7 millimeters, especially with asymmetry, is strongly suggestive of pathologic dilatation This is characteristic of optic nerve glioma, although it is also caused by neuro fibromatosis, meningioma or retinoblastoma in the orbit

The exact meaning of the dilated foramen has not been documented in the literature by a study of the soft tissue in the optic canal — nor does any of our cases furnish pathologic material from which precise conclusions can be drawn We must, therefore, interpret the significance of the dilated foramen in terms of the statistical effect upon the clinical behavior of such tumors

Twenty three of 53 patients presented with exophthamos which implied tumor in the orbit All of these showed a dilated optic foramen Fifteen of these were treated by Kroenlein orbitotomy alone with excision of the optic nerve mass Follow up periods range from 16 11, 10, 10 years and shorter periods Only in one instance has there been evidence of further disease and this occurred in a patient operated at the age of 6 months — a time when the Kroenlein procedure is technically difficult In two additional patients, on the basis of a surgeon's report of tumor at the apex radiation also was given, these patients are well at 4 and 15 years Another patient was treated by exenteration and is well after a period of 16 years One patient treated by radiation showed later intracranial recurrence and another following radiation has been well for 11 years Two patients with evidence of intracranial disease were treated by radiation — one showing continuing disease and one doing well at 6 years One patient treated at

SUMMARY — (*Contd*)

Patient	*X ray Findings**	*Treatment*	*Follow-up*
A K	9	Combined	14
	neg		
C A	5	Kronlein (Tumor at apex)	15
	7	Radiation	
S C	5	Kronlein (Tumor at apex)	4
	5 × 6	Radiation	
A S	8	Kronlein Craniotomy	8
	4	Ventriculo-pleural shunt	
		Craniotomy	
R H	—	Biopsy-canthotomy	16
		Exenteration	
M Mc	7	Radiation Craniotomy	14
	—	Enucleation V P shunt	
M M	6 5	Radiation	2
		Kronlein	
F B	8	Radiation	11
	N		
G E	large	Radiation	apathetic drowsy
	—		
	(v shaped sella)		
W R	N	Radiation	6
	large		
	(eroded clinoids)		
		VISUAL DEFECT (without proptosis)	
L B	11	Craniotomy (subtotal excision)	22
	5	Radiation	
		Kronlein	
J B	8	Craniotomy	4
	6	Radiation	
	(sella gourd shaped)		
J A	Ventriculogram	Radiation	3
	ICT		
I Br		Radiation	9
	J-shaped	Craniotomy	
L Bo	—	Radiation	Terminal
D C	NOF	Radiation	10
	sella enlarged		
L C	PEG	Craniotomy	0
	indentation	Radiation	
	floor III v		
R F	10	Craniotomy	0
	5	Radiation	
	(PEG—neg)		
R F	Ventriculogram	Radiation	5
	Hypothalamic Tumor		
R F	Large sella	Radiation	18
R G	J shaped sella	Craniotomy	Died
J G	Sella distorted	Radiation	Died
	OF large		
W J	PEG	Craniotomy (subtotal excision)	0
	vent large	Radiation	

* Skull changes sizes of foramina etc

Care must be taken to maintain proper orientation of the specimen for study by the pathologist The proximal end of the tumor should be

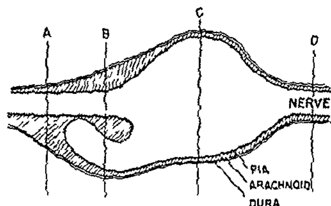


Fig 1 SCHEMA OF OPTIC GLIOMA

studied microscopically and only if actual glioma is present at this end is craniotomy indicated If the glioma portion of the tumor has been completely excised there is no need for further treatment

SUMMARY
PRESENTING WITH PROPTOSIS

Patient	*X ray Findings**	*Treatment*	*Follow up*
D C	5 6	Kronlein	3 yrs 1 & W
L C	6 10	Kronlein	7
K D	5 b	Kronlein	5
C L	5 × 6 7	Kronlein	7
G M	—	Kronlein	1
V N	–	Kronlein	2
D P	—	Craniotomy — neg Kronlein	1
R R	8 × 8 5 × 6	Kronlein	16
V S	6 × 7 4 × 5	Kronlein	10
R S	5 5 4 5	Kronlein	,
C U	foramen changes	Antrotomy Orbitotomies — neg Kronlein	13
N V	6 8	Kronlein	14
L C	5 6 5	Kronlein	6

* Skull changes sizes of foramina etc

SUMMARY — (*Contd*)

Patient	*X ray Findings**	*Treatment*	*Follow up*
A K	9 neg	Combined	14
C A	5 7	Kronlein (Tumor at apex) Radiation	15
S C	5 5 × 6	Kronlein (Tumor at apex) Radiation	4
A S	8 4	Kronlein Craniotomy Ventriculo-pleural shunt Craniotomy	8
R H	—	Biopsy-canthotomy Exenteration	16
M Mc	7 —	Radiation Craniotomy Enucleation V P shunt	14
M M	6 5	Radiation Kronlein	2
F B	8 N	Radiation	11
G E	large — (v shaped sella)	Radiation	apathetic drowsy
W R	N large (eroded clinoids,	Radiation	6
	VISUAL DEFECT (without proptosis)		
L B	11 5	Craniotomy (subtotal excision) Radiation Kronlein	22
J B	8 6 (sella gourd shaped)	Craniotomy Radiation	4
J A	Ventriculogram ICT	Radiation	3
L Br	J shaped	Radiation Craniotomy	9
I Bo	—	Radiation	Terminal
D C	NOF sella enlarged	Radiation	10
L C	PEG indentation floor III v	Craniotomy Radiation	0
R F	10 5 (PEG—neg)	Craniotomy Radiation	0
R F	Ventriculogram Hypothalamic Tumor	Radiation	5
P F	Large sella	Radiation	18
R G	J shaped sella	Craniotomy	Died
J G	Sella distorted O F large	Radiation	Died
W L	PEG vent larg	Craniotomy (subtotal excision) Radiation	0

* Skull changes sizes of foramina, etc.

SUMMARY — (Contd)

Patient	X ray Findings*	Treatment	Follow-up
A L	PEG suprasellar tumor O F large	Radiation	4
F N	Ventricles dilated	Craniotomy Torkilsen	Died
C P	PEG tumor glioma invading chiasm III ventricle	Radiation	4
J T	3 × 5 7 × 8	Radiation	4
		STRABISMUS	
I H	large	Kronlein	2
J H	tumor '	Radiation	0
L B	Large N thin dorsum	Radiation	2
I B	J shaped sella	Radiation	1
E G	Ventricles non filling	Radiation	10
I G	5 9 asymmetrical ventricles	Radiation	Died
J I	V shaped sella Large foramina	Ventriculo pleural shunt Radiation	0
S M	PEG suprasellar mass	Radiation	Died
	SYMPTOMS OF INCREASED INTRACRANIAL PRESSURE		
J A		Craniotomy	Died
D I	Dilated lateral ventricles	Radiation	14
R R	Erosion clinoids	Craniotomy Radiation	Died
H N	Dorsum destroyed	Craniotomy Torkilsen	Died
		NYSTAGMUS	
A C	8 8	Radiation	7

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THE CARDONA KERATOPROSTHESIS
FIRST CLINICAL EVALUATION

by

HERNANDO CARDONA*

RAMON CASTROVIEJO†

A GERARD DeVOE‡

Prosthokeratoplasty is the surgical procedure indicated to restore vision when a keratoplasty with either fresh or preserved donor material offers no probabilities of success In these seemingly hopeless cases a prosthetic corneal implant is the only possible means of achieving any degree of temporary or permanent visual improvement.

BRIEF HISTORY OF PROSTHOKERATOPLASTY

An artificial cornea was used in one of the first attempts made to improve vision in an eye with corneal opacities In 1771 Pellier de Quengsy (1) proposed that glass be substituted for opaque corneas His idea was implemented during the nineteenth century by Nussbaum (2) in 1853 Heusser (3) in 1859 Von Hippel (4) in 1877 and Salzer (5) who used a glass keratoprosthesis in 1898 In 1891 Dimmer (6) used a celluloid plate instead of glass Further attempts to use artificial corneas were made in 1930 by Verhoeff (7) who used a quartz button More recently Dorzee (8) Wunsche (9), Kuwabara and associates (10) Gyorffy (11) Franceschetti (12), Vanysek (13) MacPherson and Anderson (14), Stone and associates (15–16) Barraquer (17) and others have used different types of acrylic corneal implants

The experimental work with keratoprostheses carried out by Stone and his associates at the Ophthalmic Plastics Laboratory of the Massachusetts Eye and Ear Infirmary over the past twelve years deserves to be reviewed at length because they established the basic principles that made possible the definite retention of a plastic implant in a rabbit cornea In 1953 and again in 1955 Stone reported experimental studies with different models of corneal implants made of annealed methyl methacrylate (15–16) Best results were obtained with

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an implant 12 0 mm in diameter and 1 5 mm thick at the center It had numerous peripheral holes that Stone hoped would trigger the proliferation of scar tissue through the holes and that *in turn this* proliferation would lessen the tendency to extrusion A limbic incision was made, followed by an interlamellar dissection from limbus to limbus The keratoprosthesis was placed in the interlamellar pocket thus created and the limbic incision closed with interrupted sutures After a post operative recovery period of variable duration, when cicatrization was sufficiently advanced, a disc 4 0 to 8 0 mm in diameter of the central corneal tissue outside the implant was excised with a trephine Some of these trephined holes remained patent for a maximum of eight months In 1958 Stone (18) reported additional data on his experimental work with rabbits The results proved that the interlamellar implants of his design, with multiple holes to allow for tissue growth, could be maintained indefinitely by a rabbit eye with no tendency to extrusion and that holes trephined in the cornea outside the disc will remain patent for indefinite periods until the natural death of the animal The longest period of observation reported was 38 months The center of the plastic disc must be raised 1 0 mm to prevent closure of the trephined area of external cornea over the disc If this central nubbin is not raised the hole will close

Once Stone had established the feasibility of indefinite retention of the plastic implant in place by means of patent trephined holes it was necessary to devise a method to make the hole in the corneal layers posterior to the disc and maintain its patency To this end he designed an instrument with a rotating circular cutting blade that fits behind the cornea in the anterior chamber The blade was motivated remotely by a series of watch gears This third stage of the surgical procedure to incorporate an artificial cornea in a rabbit eye, the excision of the corneal layers posterior to the disc, was performed with the instrument just mentioned one or more months after the disc had been placed in the eye and the anterior trephine holes made According to Stone, if the operation is performed with a minimum of trauma and little bleeding into the anterior chamber, patency is indefinite if the hole does not close within the first ten post operative days

Five photographs illustrate this most interesting article by Stone with its many ingenious ideas They show plastic discs in rabbit eyes with holes trephined in the center of the external layers and in the center of the internal layers of corneal tissue The maximum period of observation until the natural death of the animal with both anterior and posterior trephined openings patent in the same rabbit eye was 34 months for the anterior trephined hole and 29 months for the posterior trephined hole Neither the ingenious instrument designed by Stone nor the operation is described The author stresses the use of only the purest plastic material as a prime requisite for a successful outcome His work in this field is without doubt of great value because he established for the first time the basic principles that must be incorporated in the design of a keratoprosthesis, namely

(1) An interlamellar skirt or plate to prevent extrusion,

(2) An anterior central projection in the trephined area to prevent the corneal tissue from proliferating over the face of the implant and

(3) The use of the purest plastic material available for the manufacture of the keratoprosthesis

Stone also established that the surgical approach must be through a peripheral limbic incision with dissection of an interlamellar pocket as near descemet s membrane as possible

CARDONA S EXPERIMENTAL WORK

After a careful review of the previous work on artificial corneas Cardona concluded that the through and through keratoprosthesis offers the greatest probabilities for obtaining visual improvement but the high percentage of extrusions makes the clinical application of this type of implant impractical The interlamellar keratoprosthesis gives the best promise for long or indefinite periods of tolerance with no tendency to extrusion Thus the logical design for a successful keratoprosthesis should combine the through and through optical cylinder for visual purposes and an interlamellar plate to support the cylinder and lower the extrusion rate The optical cylinder must project anteriorly as advocated by Stone to prevent corneal tissue from growing over the implant but it must also project posteriorly for the same reason The size of the supporting plate should be reduced to a minimum to lessen surgical trauma but, at the same time to prevent extrusion of the implant sufficient diameter must be preserved The clinical application of the three stage procedure proposed by Stone although very ingenious and feasible for experimental work with healthy animal corneas would be impractical A more simple operation should be devised to bring it within the realm of the average ophthalmic surgeon Since Stone only mentions the use of an instrument with a cutting blade that is introduced inside the eye to make the posterior corneal perforation but fails to describe either the instrument or the surgical maneuver used, it is impossible to judge the merits of either one It is difficult however to picture the instrument as very effective in the performance in what Stone describes as the cutting of the posterior disc because the manipulation of any instrument no matter how delicate inside an eye likely to require this type of surgery – an eye with no anterior chamber in the process of vitreous prolapse and the eye itself in a state of collapse — would be very near impossible The operation to be useful clinically must be a simple one preferable a one stage procedure and not a two or three-stage operation as advocated by Stone in the report of his experimental work

The plastic material used in the manufacture of the keratoprosthesis should naturally be the purest available, prepared and sterilized with the utmost care to insure tolerance by the corneal tissue of the host Cardona carried out extensive experimental work in rabbit eyes

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at the Nine East Ninety First Street Hospital under the direction of Dr Ramon Castroviejo Its purpose as already stated was to evaluate in an adequate number of patients the tolerance of human corneal tissue to the implant and the possibility of obtaining either temporary or permanent visual improvement The patients selected all had badly scarred corneas or eyes in which other types of keratoplasty had failed and the grafts had become either very cloudy or opaque Their vision was limited to light perception and projection hand motion or counting fingers at very close range They were all well within the limits of legal blindness

Two sizes of keratoprosthesis were used (Fig 2) one with an optical cylinder 1 5 mm in diameter (Fig 2-A) and an anterior projection of 0 65 mm and posterior of from 1 5 mm to 1 8 mm to conform to the greater thickness of the diseased human corneas as compared to that of normal rabbit corneas The interlamellar plate has a diameter of 3 5 mm The second prosthesis (Fig 2-B) has an optical cylinder 2 0 mm in diameter The anterior and posterior projection measurements are the same In this implant however the interlamellar plate has a diameter of 4 2 mm

The optical cylinder contains four elements to alternate the refraction index by correcting the spheric chromatic, lineal and field aberrations The dioptric power varies from +43 to +63 and is calculated approximately according to the size of the globe and whether or not the eye is aphakic The positive peripheral and polarization dielectric properties are changed to negative by means of an inductor manufactured by the General Electric Company

The plastic material is tested by inclusion in rabbit corneas for over six months It is used only if it does not cause any tissue reactions an indication that it is neutral and well polymerized Before surgery the prosthesis including the ocular cylinder and the supporting interlamellar plate is washed in pHisoHex liquid soap and sterilized by immersion in Zephiran solution 1 750 for 48 hours, followed by exposure to ultraviolet light for thirty minutes

PROSTHOKERATOPLASTY: SURGICAL TECHNIQUES

The patients included in this study were divided into two series according to whether the cornea was avascular or profusely vascularized FIRST SERIES — Avascular corneas The original Cardona technique as described in the report on his experimental work in normal rabbit corneas was used in 32 eyes with only minor modifications considered desirable to increase operative efficiency because of the pathologic changes in the human eyes They were affected either with bullous keratopathy secondary to cataract extraction or had undergone several keratoplasties that had resulted in a cloudy or opaque graft.

This procedure (Fig 3) performed as follows will be called Technique No 1

testing eighteen prototypes of plastic implants of different shapes and sizes. Interlamellar discs with no anterior or posterior projection were used but the results were poor and the experiments proved that proliferating corneal tissue would cover the disc unless the plate projected beyond the surrounding host cornea. A basic design with a through and through optical cylinder with a supporting interlamellar plate gave the best results. The interlamellar plate supporting the optical cylinder was then reduced in size. Cardona found that the smaller plate was as effective in preventing extrusion as the larger plate that extends over the whole diameter of the cornea, with the added advantage of reducing the surgical trauma inherent in its insertion. Non perforated interlamellar plates were easier to make and appeared to perform as well as the perforated ones, so the implants were made with non perforated interlamellar plates. The final keratoprosthesis used in rabbit eyes has an interlamellar supporting plate 3.5 mm in diameter and an optical cylinder 3.5 mm in diameter (Fig. 1). The optical cylinder projected 0.3 mm beyond the interlamellar plate both anteriorly and posteriorly.

Many acrylic materials were tested before the final selection was made. The plastic chosen contains two polymers, both polymerized by the action of light. It contains neither propionates nor cyanides, toxic substances present in most commercial acrylic plastics to which corneal cells are extremely sensitive.

The one stage surgical procedure selected as the most practical is relatively simple. A corneal incision is made near the limbus and the cornea split to make a central pocket with an external flap of two thirds of the corneal thickness and an internal flap consisting of the remaining one third. After the corneal flaps are made the cornea is perforated with a trephine through both the external and internal flaps of the pocket. The keratoprosthesis is introduced into the pocket until the projections of the cylinder engage the trephined holes to seal the openings. The operation is finished by closing the corneal incision with interrupted sutures.

Cardona's results (19) in eighty healthy rabbit eyes showed that a one stage interlamellar and through and through prosthokeratoplasty can be successfully performed and the prosthesis well tolerated for a period of up to fifteen months with no tendency to extrusion. This one stage procedure as developed by Cardona was simple enough and sufficiently tested successfully in rabbit eyes to justify a trial in very unfavorable human eyes to ascertain the tolerance of human ocular tissues to the implant and, at the same time, the possibility of obtaining by prosthokeratoplasty functional improvement in eyes that cannot benefit from other surgical procedures.

CLINICAL TRIAL

The clinical study was initiated in November, 1960, in New York at the Institute of Ophthalmology of Columbia Presbyterian Medical Center under the direction of Dr. A. Gerard DeVoe and simultaneously

(Fig 8), the margin of the corneal incision is deepened with a razor blade knife at a 45 angle away from the cornea and a total full thickness graft 0 5 mm greater in diameter than the excised host cornea is sutured to the edge of the cornea in the recipient eye with 7-0 silk sutures in approximately three fourths of its circumference The graft is not trephined in the center The Cardona mushroom prosthesis is then inserted so the cylindrical projection enters the perforation already present in the host cornea The edge of the graft not previously sutured is then closed with additional 7-0 silk sutures and the space between the graft and the recipient cornea with the Cardona mushroom prosthesis in position, is irrigated with saline solution to wash out any accumulated blood In some eyes the space between the graft and the host cornea forms an artificial pseudochamber

Another procedure Technique No 4 consisting of a split cornea with a buried mushroom prosthesis was also developed jointly by Castroviejo and Cardona (Fig 9) It was used as the original intervention in an eye with advanced bullous keratopathy secondary to cataract extraction It is performed as follows An incision is made in the cornea near the limbus in half its circumference The outer two thirds of the external layers of the cornea are dissected with the spatulated dissector over one half the cornea, including the pupillary area The anterior corneal flap is then deflected and the posterior corneal flap trephined The Cardona mushroom implant is then placed in position and the incision closed with 7-0 silk sutures This patient has been under post-operative observation for only a few weeks and the technique has been described in the full knowledge that the report is premature and the results not yet definitive However we feel that it merits presentation at this time as it may well provide the final answer to the problems of prosthokeratoplasty Should this prove to be the case its inclusion here will have served to acquaint other ophthalmic surgeons with a new procedure they may wish to investigate further

In 1953 Thomas (22) reported a buried implant similar in appearance to the one designed by Cardona The technique used to keep it in place however is different Thomas used a lamellar graft about 7 0 mm in diameter and 0 5 mm thick to secure the buried prosthesis He reported the following results Four of the six implants were retained and it was possible to examine their full depth with the slit lamp The central area in two eyes was almost clear and appeared as a small dark hole through the posterior layers of the cornea In the remaining two eyes the central area appeared slightly grey, the opacity being behind the implant

An evaluation of the results obtained in this series of 32 eyes with avascular corneas shows that in two the cornea became infected Apparently the infection was triggered in each case by a severe head cold Although the infection spread very rapidly it remained localized

(1) A Castroviejo microkeratotome (Fig 4) (20) is used to make a curved corneal incision about 9 0 mm long near the limbus The depth control mechanism is set at 0 5 mm to avoid corneal perforation (Fig 3-A) This maneuver should be monitored by a sufficiently powerful teleloupe or surgical microscope

(2) With a spatulated dissector 1 5 mm wide and 10 0 mm long (Fig 5) (21) an interlamellar pocket is made in the cornea (Fig 3-B), including the pupillary area and approximately two thirds of the anterior corneal thickness and one third of the posterior

(3) With a special trephine 1 5 mm in diameter and straight lateral surfaces, the cornea is trephined in the center, cutting through the anterior and posterior layers of the pocket (Fig 3-C) If any portion of the edge of the trephined aperture is irregular it should be trimmed with the aid of a jeweler's forceps and fine curved scissors similar to those used in keratoplasties to finish cutting the corneal discs

(4) The keratoprosthesis, held by a forceps Cardona especially designed for this purpose (a modification of Castroviejo's cross action forceps for cataract extraction) [(Fig 6)], is introduced into the interlamellar corneal pocket and the anterior and posterior cylindrical sections of the implant inserted in the corneal perforations made with the trephine (Fig 3-D)

(5) The incision is closed with 7-0 silk sutures mounted in a Castroviejo Grieshaber needle No 82-6 mm or another correspondingly fine one In a few cases 6 0 silk or catgut sutures were used (Fig 3-E)

Local anesthesia was used unless the patient was uncooperative or extremely tense

In four of the 32 eyes in which this technique was used the corneas were found to be thinner than anticipated and they did not lend themselves well to interlamellar dissection so a modified technique was developed jointly by Castroviejo and Cardona It consists in replacing the external layers of the cornea of the recipient eye with a total keratoplasty to support the through and through keratoprosthesis This procedure will be called Technique No 2 (Fig 7)

Thirty two eyes were operated using Techniques Nos 1 and 2 In five the prosthesis showed a tendency to extrude The corneal tissue external to the prosthesis in these eyes was excised over the entire surface of the cornea and replaced by a total keratoplasty The graft was trephined over the cylinder of the prosthesis to engage the external projection of the cylinder in the perforation of the trephined graft Another four eyes showed impending extrusion of the prosthesis and they were reoperated using Technique No 2 One again showed a tendency to extrusion and was reoperated for the third time Two of the remaining three were again operated using a total keratoplasty and a buried mushroom implant This will be called Technique No 3 In this procedure, developed jointly by Castroviejo and Cardona

total keratoplasty with prosthokeratoplasty Preserved corneas were used as donor material A third operation was necessary in these cases as the prosthesis again showed a tendency to extrude In the third intervention fresh corneal material was used for the total keratoplasty supporting the prosthesis In three of the five eyes operated for the third time the keratoprosthesis has been well tolerated for from fourteen to seventeen months (Fig 16) It has extruded from the remaining two and in each case the corneal aperture left by the extruded prosthesis cicatrized spontaneously by the formation of granulation tissue (Fig 17) One of these eyes was reoperated a fourth time, using a total keratoplasty of fresh corneal material to support the keratoprosthesis The implant in this eye has been tolerated for ten months

Evaluation of the results in the five eyes operated first with the original Cardona procedure (Technique No 1) followed by a prosthokeratoplasty with a total keratoplasty to prevent extrusion of the implant shows that four eyes finally tolerated the implant after a total of seventeen operations In one case when the prosthesis extruded for the third time the patient refused further surgery The present condition of his eye is the same as before surgery with vision limited to light perception and projection

Technique No 2 (total keratoplasty with prosthokeratoplasty) was used in the remaining nineteen eyes with profusely vascularized leukomas Preserved corneal material was used for the graft in four eyes and fresh in the remaining fifteen The keratoprosthesis has been well tolerated for seven and nine months in two of the four eyes in which preserved corneas were used The other two required a second operation and fresh corneal material was used for the keratoplasty supporting the implant These eyes have shown no tendency to extrusion of the prosthesis for five and seven months One of the other fifteen eyes in which fresh donor material was used developed an infection that terminated in enucleation performed elsewhere and a second was enucleated because of painful almost absolute glaucoma The keratoprosthesis has been well tolerated in an additional seven eyes although some of them already show signs of corneal erosion that may lead to extrusion They will probably require another operation Another eye was reoperated to prevent impending extrusion of the prosthesis but the cornea remaining after dissection of the granulation tissue over the implant was so thin and friable that it could not support the prosthesis and Cardona's original technique (Technique No 1) was performed in the graft already sutured in the recipient eye The implant has now been tolerated for over seven months In three more eyes with impending extrusion of the implant the corneal tissue anterior and posterior to the prosthesis was highly friable It was not deemed advisable to attempt another prosthokeratoplasty in these eyes Instead, to save their integrity the entire host cornea including the prosthesis was excised and replaced by a total keratoplasty of fresh donor material In the remaining two eyes the prosthesis was about to extrude so they were reoperated using Technique No 2

in the cornea There was no response to intensive local and systemic treatment The eyes were saved by excision of the infected corneal tissue, including the implant, which was replaced by a total keratoplasty of fresh donor material The grafts in these two have become cloudy There was no functional improvement but in their present condition these eyes are again candidates for a second prosthokeratoplasty

Another eye was lost because absolute glaucoma developed, necessitating enucleation A total keratoplasty had already been performed as well as surgery for a secondary glaucoma not controlled by a combination of local and systemic medication This eye might have fared better if the glaucoma had been under control before the prosthokeratoplasty was performed Thus tension should be normalized in eyes with increased intraocular pressure refractory to medication before a prosthokeratoplasty is done

Figures 10, 11 and 12 show the results of prosthokeratoplasties twelve, seventeen and twenty-four months after the operation and Figures 13, 14 and 15 the results obtained with a mushroom implant buried under a total keratoplasty at three, six and seven post operative months

At the present time the implant is in place in 29 of the 32 eyes in this series Some of the patients have been under observation for up to 24 months although ten reoperations, using the techniques described, were required to prevent extrusion of the prosthesis Although the operations were performed in extremely unfavorable eyes, vision improved in eighteen eyes It was remarkable in some cases, in one eye reaching 20/25 for distance and Jaeger No 1 for near and in others 20/30 to 20/60

The most interesting conclusion to be drawn from the results obtained in these eyes with avascular corneas is that the prosthesis can be made to remain in position after one, two, or even three operations in a high percentage of cases with varying degrees of corneal cloudiness or opacification, if the integrity of the collagen fibers is fairly good and the corneal thickness normal or only slightly greater than normal

SECOND SERIES — Dense leukomas profusely vascularized This series included 25 eyes with profusely vascularized dense leukomas resulting from severe burns, sequela of trachoma or severe ocular inflammation Technique No 1 (original Cardona procedure) could be used in some of these eyes but in others, because of irregular thickness, the corneas did not lend themselves well to interlamellar dissection In still others the corneas were too soft and friable and they disintegrated upon manipulation with the instruments

The following techniques were carried out in these 25 eyes Technique No 1 was used in six In five the prosthesis showed a tendency to impending extrusion, only one tolerating the implant These five eyes were reoperated using Technique No 2, consisting of a

it is more difficult to use the trephine when the eye is soft If the perforation is large it is preferable to close the coneal incision and postpone the operation for several weeks or months until the eye is completely cicatrized If the perforation occurs because the cornea is thinner than was anticipated Technique No 2 consisting of a total keratoplasty and a prosthokeratoplasty, is substituted for the original Cardona technique

When the cornea is thinner than anticipated and cannot support the anterior aspect of the prosthesis it may perforate or break during the dissection of the interlamellar pocket In this case it is advisable to excise the external layers of the cornea to the limbus and proceed with the modified rather than the original Cardona technique, using a full thickness corneal graft to support the prosthesis A keratotome with micrometrically calibrated depth control (Fig 4) (20) was developed by Castroviejo to minimize the incidence of these two complications This instrument makes it possible to incise the cornea to the desired depth If it is more than 0 5 mm thick a flap of external corneal tissue capable of supporting the prosthesis in position can be dissected and the operation is finished using the original Cardona technique On the other hand should the cornea perforate when the instrument is set to cut to a depth of 0 5 mm it is not thick enough to permit the dissection of an adequate external flap In this case it is preferable to continue the operation with the modified technique using a total keratoplasty to support the implant.

If the eye is soft at the end of the operation because of fluid or vitreous loss and it is not possible to insert the external extension of the prosthesis into the perforation in the external corneal flap tension may be increased by injecting preserved vitreous or saline solution and air into the vitreous cavity A 2 cc syringe with a 30 gauge needle is introduced into the eye through the limbus for this purpo e The increased pressure in the vitreous cavity pushes the posterior corneal flap with the prosthesis into position and the external extension of the implant engages the perforation in the anterior corneal flap Usually the preserved vitreous or saline solution is injected first to normalize the intravitreous pressure The air is then injected to create the final sudden increase in tension needed to push the corneal flap outward until it contacts the external corneal flap and the optical cylinder on the implant fits into the corneal perforation

If blood accumulates between the corneal flaps after dissection of the interlamellar pocket it should be washed out with saline solution

When the cornea of a badly burned eye is trephined it is sometimes possible to visualize intraocular structures such as the lens which were not previously discernible If the lens is clear it should not be disturbed If it is opaque it may be removed at the time of the operation with a forceps (Fig 18) or delivered with a loupe (Fig 19) through a limbic incision into the posterior corneal flap Any dense cataractous or capsular remnants or a pseudomembrane behind the trephined cornea

However, the keratoprostheses in these eyes eventually showed a displacement downward with ultimate burial under the corneal graft after spontaneous healing of the external perforation with densely vascularized granulation tissue

Evaluation of the results obtained in this second series of 25 eyes demonstrates that the surgical techniques used, whether the original Cardona procedure or the modified one consisting of a keratoplasty with prosthokeratoplasty, did not influence the final outcome However, in these eyes with dense leukoma, profuse vascularization and pronounced structural alterations of the cornea, especially of the collagen fibers, the prosthesis showed a marked tendency to extrude Numerous operations were required to keep the implant in position to improve these eyes functionally In some cases, in an attempt to save the eye, the entire host cornea, including the implant, was replaced by a total keratoplasty

Of the 25 eyes with profusely vascularized corneas in which prosthokeratoplasties were performed, after a period of observation for as long as two years, the implant remains in position in seventeen eyes after a total of 41 operations Vision improved in five eyes in one patient from light perception and projection to 20/30 for distance and Jaeger No 2 for near and in four from light perception to counting fingers at two to five feet

POST OPERATIVE CARE

Neosporin ointment is applied at the end of the operation and the operated eye closed with a monocular dressing with no pressure If the fellow eye is useful it is not bandaged The patient is ambulatory during his entire period of hospitalization The operated eye is dressed daily and Neosporin ointment applied These daily dressings are continued on an outpatient basis after discharge from the hospital in three to seven days Sutures usually are removed after the third post operative week Treatment thereafter is symptomatic Daily applications of an antibiotic ophthalmic ointment with cortisone are usually continued for several months The patient is then observed once monthly for possible tendency of the implant to extrude In cases of impending extrusion the eye should be reoperated, using one of the indicated techniques already described

During the entire post operative observation period the patient is maintained on a high protein diet with therapeutic doses of vitamins and other supportive measures to improve his general condition

COMPLICATIONS

Surgical At the time of the operation the instrument used to dissect the interlamellar pocket may perforate the section of the cornea forming its posterior aspect Should this happen, if the perforation is small, the dissection should be continued until the pocket has been completed and the operation finished as originally planned although

tissue around the implant develops a total full thickness keratoplasty, using fresh donor material to support the keratoprosthesis, should be performed (Fig 23) When the perforation in an eye from which the keratoprosthesis has already extruded shows no tendency to cicatrize spontaneously with granulation tissue the corneal opening should be closed by a partial penetrating keratoplasty (Figs 24–25) before endophthalmitis develops Intensive local and systemic antibiotic treatment should be initiated and therapy continued until all danger of intraocular infection has subsided

In three of the eyes operated a thin membrane formed over the keratoprosthesis several weeks to months after surgery This was easily removed by scraping the cornea with a razor blade knife The outer edges of the cornea surrounding the implant were then trimmed slightly with a very fine, sharp pointed scissors to prevent recurrence

Fairly profuse hemorrhages occurred in two eyes with vascularized corneas at the time of operation They persisted for some time post operatively in the vitreous and a pseudomembrane of an as yet undetermined nature formed behind the implant An operation was performed in one of these eyes in an attempt to remove the pseudomembrane but the outcome was not successful The vitreous in this eye also showed permanent pathologic changes

There were no cases of luxation of the implant toward the vitreou cavity in this series of prosthokeratoplasties using the different types of corneal prostheses described

CONCLUSIONS

It may be concluded from an evaluation of the results obtained in 81 prosthokeratoplasties performed in 57 *eye that a ke a oprosthesis* implanted in a cornea with fairly good collagen integrity will be well tolerated in a high percentage of cases Remarkable functional improvement is obtained in some eyes with periods of observation of up to 24 months When a prosthokeratoplasty is performed in an eye with a densely vascularized cornea such as those seen after severe burns the keratoprosthesis is not well tolerated and extrudes in a high percentage of cases Attempts have been made in these eyes to keep the implant in position by means of a corneal graft of either fresh or preserved donor material However the graft supporting the prosthesis often degenerated within a short time It then vascularized and assumed the characteristics of the host cornea and the implant extruded unless further surgery was performed *to prevent it*

The main conclusions to be drawn from this clinical trial are that the original Cardona prosthokeratoplasty or a slightly modified technique offers a good *prognosis for* prolonged and perhaps even permanent functional improvement in eyes with fairly good integrity of the collagen fibers On the other hand in severely vascularized corneas the keratoprosthesis whether or not it is surrounded by a total full thickness graft is not well tolerated and *often* extrudes within a

may be cut using a forceps and Castroviejo synechiotomy scissors introduced through a limbic incision (Fig 20) However, a clear or cataractous lens, cataractous remnants or a pseudomembrane may be left undisturbed until the eye has completely recovered from the prosthokeratoplasty Then, in about three months, the indicated procedure should be carried out to remove any intraocular structures that interfere with vision

Post operative During the immediate and late post operative period the most serious complication encountered is infection of the corneal tissue surrounding the prosthesis (Fig 21) If an infection should develop specimens should be cultured immediately to determine the causative agent and sensitivity tests run to select the most effective antibiotic Treatment, however, should be initiated at once without waiting for the results of these tests, with applications of a broad spectrum antibiotic or a combination of antibiotic ophthalmic ointments applied alternately Antibiotics should also be administered systemically and the patient's general condition improved with a high protein diet and therapeutic doses of vitamins Intravenous injections of typhoid vaccine should be given to boost the patient's defenses As soon as the results of the sensitivity tests are known the most effective antibiotic should be administered with no further delay If the corneal infection continues to progress in spite of this intensive treatment and endophthalmitis threatens the eye, the whole cornea should be excised immediately and replaced by a total full thickness graft (Fig 22) to preserve the integrity of the eye Local and systemic treatment with antibiotics should be continued until all danger of infection has subsided

This serious complication occurred in three eyes included in this study and the treatment outlined arrested the infection Vision in these eyes has remained the same as before the initial prosthokeratoplasty They are now pending reoperation

In seriously diseased corneas with dense leukoma and profuse vascularization recurrent ulcers are a frequent complication during the immediate and late post operative recovery period after a prosthokeratoplasty They also occur in eyes in which total keratoplasties have been performed but no keratoprosthesis inserted It is possible that these ulcerations are not caused by the keratoprosthesis but result from a number of other factors precarious nutrition of the cornea, neurotropic disturbances or perhaps they are an immunologic response In spite of intensive antibiotic therapy the cornea almost always erodes in these instances and the implant extrudes unless another operation is performed Of course, reoperation offers a very poor prognosis for tolerance of the implant in these cases

By far the most frequent complication, which is more often observed in vascularized opacities, is the slow erosion of the corneal tissue surrounding the implant leading to its extrusion in two to sixteen months As soon as a seemingly progressive erosion of the corneal

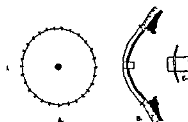


Fig 7 Castroviejo-Cardona total keratoplasty technique with through and through keratoprosthesis

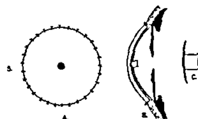


Fig 8 Castroviejo-Cardona total keratoplasty technique with buried Cardona mushroom implant

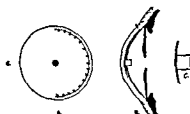


Fig 9 Castroviejo-Cardona buried mushroom keratoprosthesis technique with split cornea.



Fig 10 Keratoprosthesis in position in a human eye twelve months after the operation.



Fig 11 Keratoprosthesis in position in a human eye seventeen months after the operation.



Fig 12 Keratoprosthesis in position in a human eye 24 months after the operation.

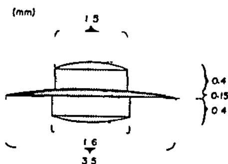


FIG 1 Drawing of Cardona's keratoprosthesis used in rabbit eyes

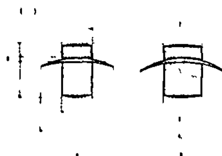


FIG 2 Drawing of Cardona's keratoprosthesis used in human eyes 2 A with an optical cylinder 1 5 mm in diameter and 2 B 2 0 mm in diameter

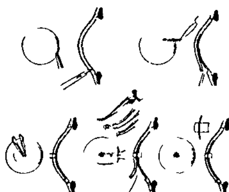


FIG 3 Cardona's prosthokeratoplasty technique with slight modifications as used in human eyes

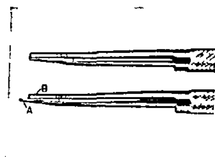


FIG 4 Castroviejo's microkeratotome with depth control mechanism for the cutting blade



FIG 5 Castroviejo's spatulated dissector

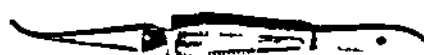


FIG 6 Cardona's forceps to hold the keratoprosthesis



Fig 20 Technique for total keratoplasty supporting the keratoprosthesis and excision of dense capsular remnants with Castroviejo synechiotomy scissors



Fig 21 Infection of the corneal tissue surrounding a keratoprosthesis following a severe head cold four months after the operation

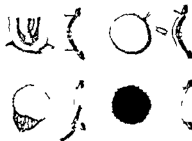


Fig 22 Treatment of an infected cornea after prosthokeratoplasty with excision of the entire cornea including the keratoprosthesis which was r placed by a total penetrat ng graft of fresh donor material

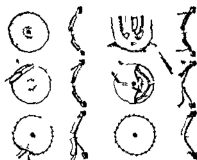


Fig 23 Treatment of corneal erosion around the keratoprosthesis with excision of the external layers of ulcerated corneal tissue and the keratoprosthesis with replacement by a full thickness total keratoplasty and another keratoprosthesis



Fi 4 Small partial penetrating keratoplasty used to close the rneal open ng after extrus on of the keratoprosthes s from a human eye



Fig 25 Human eye with a small partial penetrating keratoplasty used to close the corneal perforation after extrusion of the keratoprosthesis



Fig 13 Castroviejo Cardona buried mushroom implant supported by a total keratoplasty in position *in a human eye* three months after the operation



Fig 14 Castroviejo Cardona buried mushroom keratoprosthesis supported by a total keratoplasty *in position* in a human eye six months after the *operation*



Fig 15 Castroviejo Cardona buried mushroom keratoprosthesis sup *ported by a total penetrating kera* toplasty in position in a human eye seven months after the operation



Fig 16 Keratoprosthesis in position in a vascularized human cornea 17 months after the operation

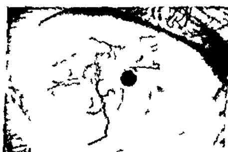




Fig 17 (A) Cardona's keratoprosthesis in position in a human eye with densely vascularized cornea (B) The same eye after extrusion of the *keratoprosthesis* and *spontaneous* closure of the corneal opening by granulation tissue



Fig 18 Technique for total keratoplasty supporting the kerato*prosthesis* and cataract extraction with forceps

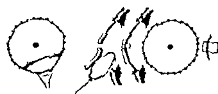


Fig 19 *Technique for total kera* toplasty supporting the keratoprosthesis and cataract extraction with *loop*

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few weeks or months, sometimes resulting in loss of the eye In these cases the use of a full thickness corneal graft to support the prosthesis may prevent this complication

Thus, for patients with an avascular cornea the original Cardona or modified prosthokeratoplasty technique seems to be a valuable addition to the field of corneal surgery However, eyes with profusely vascularized corneas must be improved structurally before they can be successfully treated by prosthokeratoplasty, performing the corneal graft first and then the prosthokeratoplasty when the eye has recovered from the first operation

The technique of the full thickness corneal graft to support the keratoprosthesis may be used in some cases as a one stage operation, particularly in patients with limited time for the entire surgical treatment but it is preferable, whenever possible, to improve the cornea structurally and postpone the prosthokeratoplasty until the eye has recovered from the first operation and is in a more favorable condition to undergo a prosthokeratoplasty

SUMMARY

The clinical trial of the Cardona prosthokeratoplasty operation is reported as well as some modifications in the techniques required by certain eyes in which the original Cardona operation could not be performed Other techniques to prevent extrusion of the implant are described The post operative care and treatment of complications are briefly outlined

The authors realize that the report of these few cases of artificial corneas will have to stand the test of time but they feel that this branch of corneal surgery has passed from purely animal experimentation to that of clinical application of these new procedures in carefully selected very unfavorable eyes They present their views in the hope that this report will stimulate the interest of other ophthalmic surgeons in this field and with the combined efforts of many arrive earlier at a more successful and lasting beneficial result from the use of artificial corneas

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For corneal grafting normal adult animals of known sexes were used as recipients and donors

Corneal heterografts of cat, mouse and bovine tissues varying in thickness and size were transplanted onto rabbits by interlamellar techniques (5) To reduce the host s immune reactions the epithelium was removed from some of the heterografts in others the heterografts were enclosed in specially made intracorneal diffusion chambers described in a previous paper (6)

Full and partial thickness corneal homografts five to seven mm in diameter, were transplanted in rabbits and cats by penetrating, lamellar and interlamellar techniques Some of the interlamellar homografts were enclosed in diffusion chambers

The grafts were removed at different postoperative periods up to a year taking sufficient care not to include any host tissues

A few full thickness and lamellar human grafts were also obtained These grafts were semiopaque and were removed for the purpose of retransplantation The ex of the donors from whom they originally came and that of the patients from whom they were removed were *different*

For cytological studies, only the transparent animal grafts and the clearest portions of human grafts were cultivated *in vitro* The sex chromatin and chromosome preparations were made from short term cultures

RESULTS

The results of various experiments will be discussed under the following headings

I THE BEHAVIOUR OF THE CORNEAL CELLS IN TISSUE CULTURE

The cultural characteristics of the cells from the different layers of the cornea viz the epithelium stroma and endothelium varied. In this respect there was also species differences The stromal cells from the corneas of all the mammalian species so far studied could be cultivated readily in the primary short and long term cultures on glass surface Adequate primary outgrowths of the corneal epithelium from all of these species were obtained These epithelial cultures could be maintained satisfactorily for periods up to four weeks But subculturing of these cells by trypsinization was difficult However, we were able to sub-culture the bovine corneal epithelium satisfactorily for three passages and in one instance that of rabbit for two passages With regard to the cultivation of the corneal endothelium, we succeeded in culturing the rabbit s endothelium but so far have obtained inconsistent results with other species With the rabbit endothelium we observed that once the cells started to grow in the

CYTOLOGICAL STUDIES ON THE CORNEA FOR AN UNDERSTANDING OF THE FATE OF THE CELLULAR ELEMENTS OF HOMO AND HETEROGRAFTS*

P. K. BASU and P. SARKAR†

This study is a part of a larger investigation on the fate of the cellular elements of corneal grafts, and deals with the karyotypes of man and a few mammalian species as studied in corneal tissues, and the cytology of some of the short term corneal grafts.

The use of cytological techniques in our research has been primarily motivated by the idea of using sex chromatin and chromosome *complements as biological cell markers for tracing the donor cells* following corneal transplantation.

Before we could apply these structures to the study of grafts, certain basic investigations had to be performed on normal corneal tissues. As we employed tissue culture techniques exclusively in making cytological preparations, it was important to know whether our *in vitro* methods had any effect on these structures. Furthermore, in view of the possibility of variation of chromosome number in somatic cells (1), it was also necessary to find out whether there was any such inconsistency in the corneal tissues.

METHODS AND MATERIALS

The details of the tissue culture technique and the methods used for making the sex chromatin and chromosome preparations from the tissue culture cells have been described in previous reports (2, 3, 4).

For the preliminary cytological studies various tissues viz., the cornea, sclera, retina, skin, lung and kidney were used from the rabbit, cat, cattle, mouse and man. The preparations of the sex chromatin and chromosomes were made from cells cultivated in the primary short and *long term cultures. A cell population which did not undergo* more than four passages was termed a short term culture and that which underwent more than four passages a long term culture. The passages were usually made at weekly intervals by trypsinization.

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KARYOTYPE OF THE RABBIT

The normal chromosome complement of the rabbit as observed in the corneal stromal cells is shown in figures 1 and 2



FIG 1 The chromosome complement of rabbit (in corneal stromal cell)

The chromosome number of the rabbit is 44 including the X and Y in the male and the two X s in the female The karyotype shows paired chromosomes from a typical nucleus of male It can be seen that the chromosomes fall into distinct groups with respect to total length and arm ratio The Y chromosome in the male is similar to the two smallest autosomes The X is a medium sized chromosome with arm ratio of

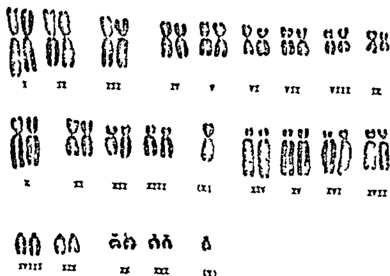


FIG 2 The karyotype of rabbit (male)

primary culture, subsequent short- and long term subculturing by trypsinization was not difficult

In tissue culture, cells from the different layers of the cornea tended to retain their individual morphological appearance, as shown in the primary outgrowth, even in long term cultures This pheno menon was observed particularly in the epithelial and stromal cells of the cattle and mouse cornea, and in the cells from all the layers of rabbit cornea (4)

2 THE EFFECT OF TISSUE CULTURE ON THE SEX CHROMATIN AND CHROMOSOME COMPLEMENTS

Satisfactory sex chromatin preparations were obtained from the different layers of the cornea of man, rabbit and cat However, due to the variation in number and distribution of heterochromatin bodies in mouse, and particularly in bovine cells, identification of the sex chromatin was difficult in these animals The percentage of cells with sex chromatin in the stromal cells of the rabbit s cornea was found to be almost constant up to the sixth trypsinized passage, at which time the experiment was discontinued

The chromosomes were satisfactorily studied in the primary, short and long term cultures of the cells from the different corneal layers of man and animals The chromosome complements were identical in the primary and short term cultures In one instance, in a long term culture of the rabbit cornea, the karyotype of the stromal cells was unaltered even up to the 27th passage

Repeated studies on the primary and short term cultures demonstrated conclusively that cells from both of these cultures were reliable for studying the normal karyotype of an animal However, it was found that the short term cultures provided better monolayer cell preparations than the primary ones Therefore, in later experi ments we used only short term cultures, and assumed that results obtained from them would be a true indication of the chromosomes of the tissue *in vivo*

3 KARYOTYPES OF THE DIFFERENT MAMMALIAN CORNEAS

In all the mammalian species studied so far, we found that cells from the different layers of cornea had identical chromosome comple ments We also observed that the karyotype of the cornea was identical with that of other tissues such as, the sclera, retina skin, lung and kidney, in the same individual

A few general characteristics of the chromosome complements of the rabbit, cat, mouse, and cattle as well as that of man are described briefly below The photomicrographs of the chromosomes were taken with oil immersion lens, and the karyotypes were made from camera lucida drawings

very great However, it has been possible to determine the sex of the animals from the chromosomes studied in the corneal tissues grown *in vitro* The X and Y pair is the second smallest in the complement (number 18) The X is almost metacentric with two equal arms, while the Y is unequally armed The chromosome number 17 is nucleolar with a conspicuous secondary construction in one of the arms There are two pairs number 15 and 16 of almost telocentric chromosomes The rest of the chromosomes can be separated into distinct groups according to size and arm ratios as shown in the karyotype (1–3, 4–6 7–8 9–10 11–16) Numbers 1 2 and 3 are individually identifiable by distinct arm ratios while the chromosomes in each of the other four groups are similar in size and morphology

Karyotype of the Cattle

The normal chromosome complement of the bull, as observed in the corneal epithelial cells, is shown in figures 5 and 6

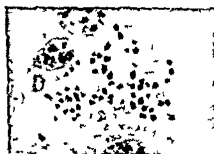


Fig 5 The chromosome complement of cattle (in corneal epithelial cell)

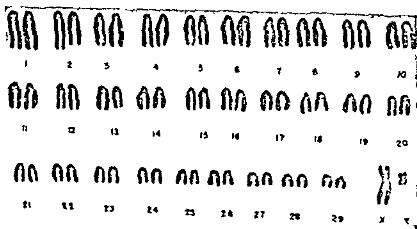


Fig 6 The karyotype of cattle (male)

approximately 1 to 3 The chromosomes numbered 18 and 19 are *distinct from the rest in being almost telocentric* (4)

KARYOTYPE OF THE CAT

The normal chromosome complement of the cat as observed in the corneal stromal cells is shown in figures 3 and 4

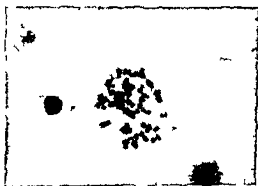


FIG 3 The chromosome complement of cat (in corneal stromal cell)

In the somatic cells the cat has 38 chromosomes The chromosomal sex determining mechanism in the cat is rather subtle in that the morphological difference between the X and Y chromosome is not

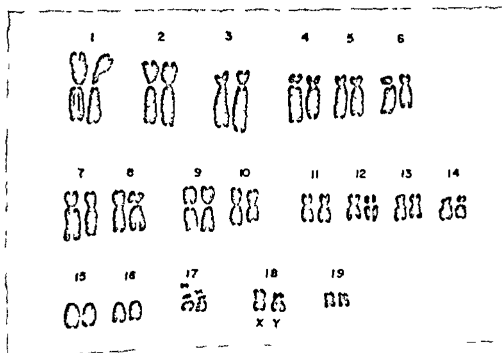


FIG 4 The karyotype of cat (male)

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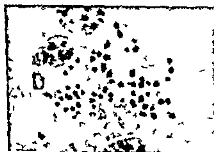


FIG 5 The chromosome complement of cattle (in corneal epithelial cell)

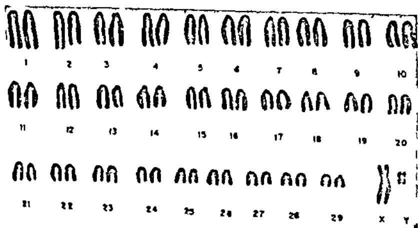


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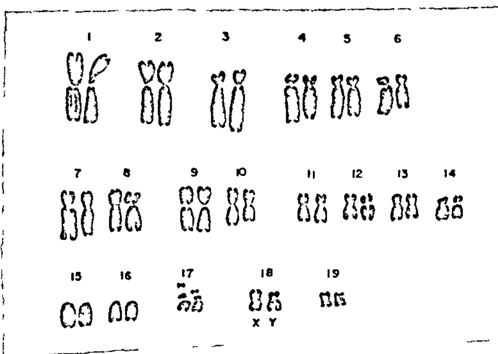


FIG 4 The karyotype of cat (male)

chromosomes we have not attempted to distinguish the sex of the mouse in our chromosome preparations

KARYOTYPE OF MAN

The normal karyotype of man, as observed in the *corneal stromal* cells is shown in figures 9 and 10

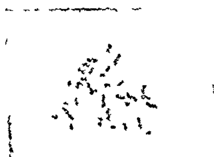


FIG 9 The chromosome complement of man (in corneal stromal cell)

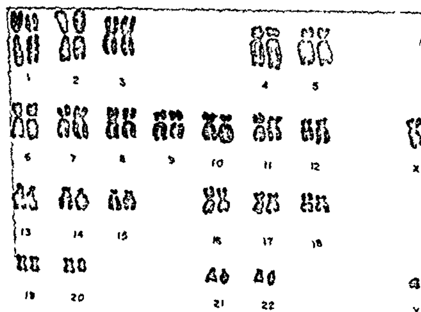


FIG 10 The karyotype of man

In figure 10 the chromosomes have been arranged according to the recommendations of the Denver Convention (7) Our results

A somatic bovine cell contains 60 chromosomes All the chromosomes except the sex chromosome are almost telocentric In addition to 29 pairs, or 58 chromosomes, the bull has an X and Y chromosome while the cow has two X's The sex chromosomes here are very easily distinguishable from the rest of the chromosomes because of their characteristic morphology

KARYOTYPE OF THE MOUSE

The normal chromosome complement of the mouse, as observed in the corneal stromal cells, is shown in figures 7 and 8



FIG 7 The chromosome complement of mouse (in corneal stromal cell)

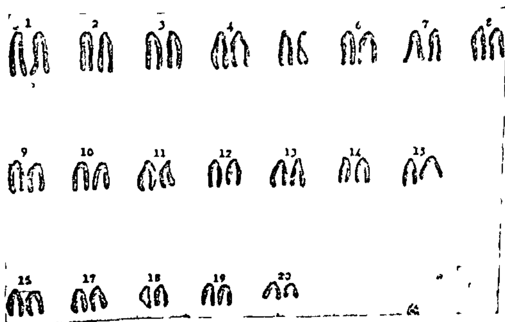


FIG 8 The karyotype of mouse (male)

The chromosome number of the mouse is 10 All the chromosomes are almost telocentric Because of the difficulty of identifying the sex

12, 13) Table 1 shows the fate of the cellular elements of some of the homografts It is interesting to note that the original donor cells of the human graft persisted up to 406 days the maximum age of a graft so far studied by us

TABLE 1 — *Fate of the cellular elements of homo- and heterologous corneal grafts*

Donor	*Host*	*Type of Graft*	*Age of Graft*	*Cell Marker*	*Identification of original Donor cells*
Cat	Cat	*Penetrating*	*306 Days*	Sex Chromatin	Positive
Rabbit	Rabbit	Interlamellar	180 Days	Sex Chromatin	Positive
Human	Human	Lamellar	406 Days	Sex Chromatin	Positive
Cat	Rabbit	*Interlamellar*	*43 Days*	Karyotype	Positive
Mouse	Rabbit	Interlamellar	52 Days	Karyotype	Positive

Karyological studies on the cells from a few human, and many animal homo- and heterografts are now progressing in our laboratory We are analysing the number and structure of the chromosomes of the graft at different postoperative periods and comparing them with the normal chromosome complement of the host and the donor

A series of cat and mouse full thickness heterografts was transplanted interlamellarly in rabbits The grafts were removed for cytological studies at intervals of about two weeks Results obtained from 43 day old cat grafts (6) and 52 day old mouse grafts showed that the original donor cells were viable and cytologically normal *Table 1* Figures 14 15)

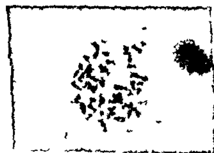


Fig 14 The chromosome complement of a cat corneal heterograft transplanted in a rabbit for 43 days Metaphase showing 38 chromosomes



Fig 15 The chromosome complement of a mouse corneal heterograft transplanted in a rabbit for 52 days Metaphase showing 40 chromosomes

show that the human karyotype as studied in the corneal cells is identical with that from other somatic cells (8)

4 THE SEX CHROMATIN AND CHROMOSOME COMPLEMENTS OF CORNEAL GRAFTS

As stated earlier, only clear animal grafts and the most transparent portions of the human grafts were used for culturing, and subsequent cytological analysis Histological studies made from the remaining portions of the grafts did not reveal any abnormality excepting a few scattered round cells in the human grafts

The sex chromatin was studied in the cells of a number of homo grafts (human, rabbit and cat) which were transplanted to recipients belonging to the sex opposite to that of the donors By estimating the percentage of cells containing the sex chromatin in a cell population derived from the grafts, the sex of the tissue was determined (Figs 11,



FIG 11 The nucleus of a cell from a cat corneal homograft showing the sex chromatin The graft came from a female donor and was in a male host for 306 days

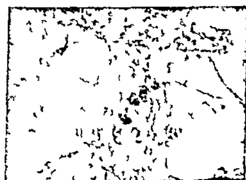


FIG 12 The nucleus of a cell from a rabbit corneal homograft showing no sex chromatin The graft came from a male donor and was in a female host for 180 days



FIG 13 The nucleus of a cell from a human corneal homograft showing no sex chromatin The graft came from a male donor and was in a female host for 406 days

graft (which may be called a 'tissue culture *in vivo*') in adapting themselves to a new surrounding would undergo any cytological changes comparable to the behaviour of a cell population *in vitro*

In our experience different corneal cells *in vitro* appeared to be resistant to any morphological and karyological changes in long term culture This suggested that the cells of a corneal graft might also show a similar tendency As mentioned earlier, we have not been able to detect any karyological changes in the few short term heterografts so far studied

SUMMARY

1 This report deals with the cytology of the normal and grafted corneas of a few mammalian species including man

2 In serial culture cells from the different layers of the cornea tend to maintain their characteristic morphology and cytology

3 The origin of a tissue can be determined by using the sex chromatin and chromosome complements as biological cell markers These structures are very satisfactorily seen in cells cultivated *in vitro*

4 The karyotypes of the rabbit cat cattle mouse and man as studied in normal corneal cells are described

5 Initial results show that in corneal homo- and heterografts the original donor cells remain viable and cytologically unaltered for a prolonged period (in one instance of a human homograft even for more than a year)

ACKNOWLEDGMENT

We are grateful to Dr George A Thompson who kindly supplied us with the human corneal grafts and to Miss I Miller and Mr F Carré for their technical assistance

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DISCUSSION

The present progress in the field of mammalian cytology has been largely possible due to the adaptation of tissue culture techniques for making better cytological preparations In our studies on the cytology of corneal cells, these techniques have proved to be of great value (2, 4)

In this and in previous studies (3), we have successfully used the sex chromatin as a biological cell marker in the study on the fate of corneal grafts In the use of sex chromatin, however, certain limitations should be considered This method is dependent on a very delicate staining procedure as well as on a precise determination in a cell population of the percentage of cells with sex chromatin It is obvious that in unsuitable preparations, or in the presence of multiple hetero chromatin bodies, as in bovine corneal cells (Fig 16) the correct



Fig 16 Nuclei of corneal stromal cells of cattle showing multiple heterochromatin (DNA positive) bodies

assessment of the frequency of the cells showing sex chromatin can be very difficult The percentage of cells with sex chromatin may also vary over a wide range in different species Under certain conditions female cells may not even exhibit it, whereas in others, the cells may show duplicate bodies (9)

We thus feel that karyotypic studies give a more precise information about the sex and species of a cell population Furthermore, these studies enable one to locate any genetic changes expressed in the form of structural alterations of the chromosomes

With respect to the dispute about the constancy of the chromosome number in somatic cells (1), from our studies we were able to establish that the karyotype of the corneal tissue was identical with that obtained from other somatic tissues in the same species

It is well known that many kinds of mammalian cells undergo morphological and cytogenetical changes on long term cultivation (10) Therefore, we were also interested to see whether the cells of a

The eye was irrigated with normal saline and the corneal scrapings were inoculated into Czapek or Sabouraud's medium and kept at the laboratory temperature A portion of the scrapings was stained with lactophenol cotton blue and examined for the presence of hypae or spores In the last ten of this series, corneal scrapings were suspended in 5 c c of sterile distilled water Four culture plates were inoculated with one drop of suspension each For every case all the four plates had the growth of the same fungus Under identical conditions in the laboratory, a sterile culture plate of Czapek medium was opened



I (Czapek Medium) Culture plate showing the growth of Actinomyces Draeli



II Actinomyces israeli × 400 granule stained by Lactophenol Cotton blue



III Fusarium Culture plate Czapek Medium



IV Fusarium × 400

for ten seconds and closed at the same time There was no growth in this plate A drop of fluorescein kept for routine use in the out patient was inoculated into a Czapek medium. In another plate of same medium the nozzle of ointment tube used for patients was touched

MYCOTIC KERATITIS

E BALAKRISHNAN,

Government Ophthalmic Hospital, *Madras, India*

Hajano (1910) reported a case of hypopyon ulcer caused by Aspergillus fumigatus from Japan R H Elliot (1920) stated that during *his term of office as superintendent, Government Ophthalmic Hospital,* Madras met with several cases of fungoid infection of the cornea Makby Kissen and Sine stated that the first case of keratomycosis was recorded in 1933 at the Armed Forces Institute of Pathology Two more cases were recorded in the next nineteen years and between 1952 to 1956 thirteen more cases were added Quentin (1937) and Tsutsui (1957) recorded two cases of corneal ulcers caused by Clostridium Tetani Sigtenhorst and Gingrich reported one case of Nocardia Asteroides Anderson B Roberts and others (1959) have reported four cases of mycotic ulcers Wendell and Gingrich and Mary E Pinkerton of Texas (1962) reported a case of corneal ulcer caused by Actinomycosis bovis

In the Government Ophthalmic Hospital, Madras, on an average, three hundred and eighty nine cases of hypopyon ulcers are admitted annually In the last two years (October 1960 to November 1962) sixty of them were clinically suspected to be of mycotic origin and thirty of them were confirmed by culture All the patients were adults, twenty of them were males and ten females All the patients with hypopyon ulcers were working on the farm when the eyes were injured by corn stalk or haystalk or dust from the soil or chips of wood After a few hours of injury they had symptoms of watering and photophobia, and sought admission after an interval of about six days in average None of them had local cortisone or antibiotics and all of them had well established hypopyon ulcers on admission After examining the lacrimal passage, routine treatment of subconjunctival penicillin, atropine drops and antibiotic ointment was given and the eyes were bandaged Systemically sulpha tablets or strepto penicillin were administered for one week Cases which did not respond were reviewed and the presence *of any one of the following signs was taken as suspicious* of mycotic ulcer

1 The ulcer being faintly yellow in colour, with beaded border
2 Dark brown or black pigments on the floor of the ulcer
3 The presence *of a hypopyon even when the ulcer is of small* size
4 Secondary glaucoma

The eye was irrigated with normal saline and the corneal scrapings were inoculated into Czapek or Sabouraud's medium and kept at the laboratory temperature A portion of the scrapings was stained with lactophenol cotton blue and examined for the presence of hypae or spores In the last ten of this series, corneal scrapings were suspended in 5 c c of sterile distilled water Four culture plates were inoculated with one drop of suspension each For every case all the four plates had the growth of the same fungus Under identical conditions in the laboratory a sterile culture plate of Czapek medium was opened



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for ten seconds and closed at the same time There was no growth in this plate A drop of fluorescein kept for routine use in the out patient was inoculated into a Czapek medium In another plate of same medium the nozzle of ointment tube used for patients was touched

All the plates were incubated at the laboratory temperature and there was no growth in any of these plates These investigations proved that the cases were *not of secondary* contaminants

An analysis of mycotic infection collected in two years

TABLE I

Total No of cases	Males	Females
30	20	10

TABLE II

Hypopyon Ulcers	Granuloma following evisceration	Canaliculitis (lower)
24	4	2

TABLE III

Name of fungi cultured	*From corneal ulcers*	*From granuloma*	*From canaliculus*
Aspergillus fumigatus	13	3	2
Genus Aspergillus		1	
Actinomyces Israeli	2		
Mycelia Sterilans	3		
Blastomyces dermatitis	2		
Helmenthosporium	1		
Fusarium	1		
Unknown fungi	2		

TREATMENT

Antifungal ophthalmic ointment was not available and so it was not tried The ulcer was cauterised with iodine, mydriatic applied locally and bandaged Every day the eye was irrigated gently with saline, Nystatin tablets of Squibbs (Mycostatin I Tab = 500,000 units) one tablet t d s for fifteen days was given Secondary glaucoma was controlled with diamox tablets Paracentesis was not done

COMPLICATIONS

In almost all the cases secondary glaucoma is the commonest complication during treatment In five cases the ulcer perforated and the prolapsed iris was cauterised by electric cautery The vascularization of the cornea was not seen in the early stage of the ulcer, but was noted in the late cases However it was not prominent, and could be detected only by a slit lamp Complicated cataract could be detected in two of the cases of ulcer due to Aspergillus fumigatus



V Helmenthosporium × 400



VI Corneal Scraping Unknown Fungus × 400



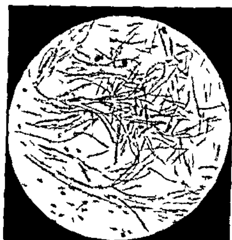
VII Aspergillus fumigatus × 600

RESULTS

Out of these thirty cases, marked visual improvement was noted only in four of them 6/36 to 6/12 Rest had perception of hand movements due to dense leucomas In spite of the treatment five ulcers perforated followed by usual complications In almost all cases of ulcers due to Aspergillus fumigatus the pain was relieved and hypopyon was observed within forty-eight hours after administration of mycostatin

GRANULOMA FOLLOWING EVISCERATION

Annually about one hundred cases of panophthalmitis were admitted and eviscerated During the last two years four of them developed granulomatous mass inside the scleral coat after evisceration, with recurrence of pain and oedema of the lids In the early stages, the granuloma was soft, later firm and infiltrating into the sclera, when dissected out there was bleeding Three of these cases were due to Aspergillus fumigatus and one was of genus Aspergillus and its species could not be identified



VIII Mycelia Sterilans × 400

CANALICULITIS

Two cases were of canaliculitis of lower canaliculus due to Aspergillus fumigatus and they were relieved after repeated syringing with penicillin solution

DISCUSSION

All the hypopyon ulcers occurred in farmers, after minor trauma to the eyes while working in the fields Pathological fungi cultured from all these cases were proved to survive in the soil (Emmons 1951 and Gohar 1948) So it is inferred that these cases were of primary infection carried from the soil to the cornea due to minor injuries Sufficient investigations were done to prove that they were not of contaminants from the fluorescein or from the nozzle of the ointment tube commonly used, or from the atmosphere of the laboratory It is to be noted that in all these cases there was no previous treatment with antibiotics or with corticosteroids

Due to the absence of specific anti fungal agents, treatment of these cases were not satisfactory Nystatin and Griseofulvin were the only drugs available in South India Griseofulvin has no action on the fungi cultured in these cases Nystatin was therefore administered Ulcers caused by Aspergillus fumigatus, Blastomyces and Helmenthosporium responded well The exotoxin of Aspergillus fumigatus

seems to have been neutralized by Mycostatin administered orally Blastomyces and Helminthosporium also seem to secrete exotoxin since they responded well to the systemic administration of Nystatin Fusarium mentioned in this review was grown on Czapek medium The identification was based on the appearance of spores which were sickle shaped with pointed ends and with cross septa Helmenthosporium was grown on potato dextrose medium Its spores were long roughly cylindrical somewhat attenuated at ends Actinomyces Israeli was grown on Czapek medium The growth was very slow, the colonies were snow ball like The hyphae were about one in in diameter and were branching They were gram positive and non acid fast When cultured by Henrici method the granules were very small, yellowish white in colour and were visible to the naked eye Under the microscope they were polygonal in appearance with a tangle of filaments in the centre They gradually opened out in periphery as clubs' which were acidophilic

This review brings out the urgent necessity for the search of specific anti fungal agent to reduce the incidence of blindness due to hypopyon ulcers in the agricultural workers

The fungi reported in this study were cultured and identified by Dr T K R Reddy M Sc P H D a mycologist under the guidance of Professor T S Sadasivam of Botany Laboratory Madras University I should thank Dr T T Ramalingam, Superintendent of Government Ophthalmic Hospital and Professor Anantharaman Head of the Department of Parasitology Madras Veterinary College for their useful suggestions I am grateful to Dr (Miss) Manikar M D, Director of Medical Services of Madras for deputing me to read this paper at the XIX International Congress of Ophthalmology, New Delhi

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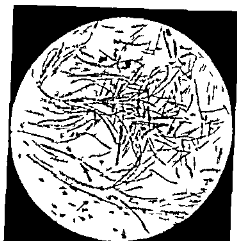
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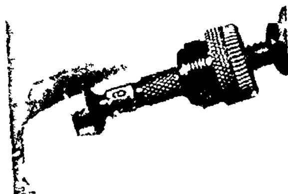
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scrapped and is planted in 9 day embryonated chicken egg for 48 hours This can be done in human cornea in vivo or in cadaver eyes or even



Fi 1 Solid Piston of Castroviejo corneal trephine



Fi Appearance of Chicken Cornea immediately after it is frozen with solid piston of Castroviejo corneal trephine soaked in CO snow absolute alcohol mixture



Fig 3 Appearance of Chicken Cornea 5 seconds after application of frozen solid piston clear as before



Fig 4 Normal Cellular Cornea

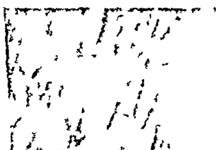


Fig 5 Acellular Cornea

ARE THE NON CELLULAR PORTIONS OF THE CORNEA VIABLE?*

GEMINIANO de OCAMPO, ROMEO B ESPIRITU, SALVADOR R SALCEDA

Manila, Philippines

Frozen or unfrozen glycerin dehydrated corneas used for lamellar keratoplasty preserve their transparency although none of their cells grow in tissue culture (7) When these corneas are embryonated their cells disappear leaving acellular cornea (5) This further shows that their cells were dead It is claimed that this dehydrated cornea with dead cells is not viable and hence viability of the graft is not necessary for successful lamellar keratoplasty This is premised on the concept that *the non cellular portions of the cornea are non viable* However, this is open to doubt because certainly this dehydrated cornea graft with dead cells does not maintain its transparency like an inert acrylic graft The question is therefore asked, 'Are the non cellular *portions of the cornea viable?*" *To answer this question is the* purpose of this communication

Almost all previous works on corneal viability have been done on cornea with cells It seems that by " corneal viability " is meant ' corneal cell viability " which is based solely on culture cell growth In a previous communication we urged a re examination of *this concept*(2) If the cells from the cornea can be removed and the remaining portions studied as to its properties, this question can be enlightened further This would be a step forward in the study of corneal grafting as well as in other branches of *tissue transplantation* where the *non cellular structures* are considered dead(8)

How an acellular corneal graft is made To the cornea in vivo and in situ is applied the solid piston of the Castroviejo corneal trephine (Fig 1) after it has been soaked in carbon dioxide alcohol solution to acquire a temperature of—49°C The cornea becomes white (Fig 2) and *in a few minutes resumes its former* transparency (Fig 3) After 48 hours the cornea looses its stroma cells By scrapping the epithelium and endothelium, this cornea becomes completely acellular This procedure can be repeated with the same result if after *instantaneous freezing*, the cornea is removed, its epithelium and endothelium

* Read before the 19th International Congress of Ophthalmology at New Delhi, India Dec 1962

Supported by a grant from the NSDB and UP

scrapped and is planted in 9 day embryonated chicken egg for 48 hours This can be done in human cornea in vivo or in cadaver eyes or even

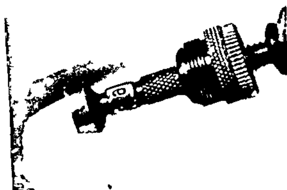


Fig 1 Solid Piston of Castroviejo corneal trephine



Fig 2 Appearance of Chicken Cornea immediately after it is frozen with solid piston of Castroviejo corneal trephine soaked in CO_2 snow absolute alcohol mixture



Fig 3 Appearance of Chicken Cornea 5 seconds after application of frozen solid piston clear as before

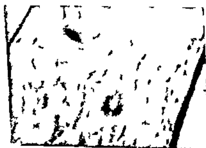


Fig 4 Normal Cellular Cornea

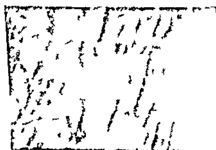


Fig 5 Acellular Cornea

ARE THE NON CELLULAR PORTIONS OF THE CORNEA VIABLE?*

GEMINIANO de OCAMPO, ROMEO B ESPIRITU, SALVADOR R SALCEDA

Manila, Philippines

Frozen or unfrozen glycerin dehydrated corneas used for lamellar keratoplasty preserve their transparency although none of their cells grow in tissue culture (7) When these corneas are embryonated their cells disappear leaving acellular cornea (5) This further shows that their cells were dead It is claimed that this dehydrated cornea with dead cells is not viable and hence viability of the graft is not necessary for successful lamellar keratoplasty This is premised on the concept that the non cellular portions of the cornea are non-viable However, this is open to doubt because certainly this dehydrated cornea graft with dead cells does not maintain its transparency like an inert acrylic graft The question is therefore asked, 'Are the non cellular portions of the cornea viable?" To answer this question is the purpose of this communication

Almost all previous works on corneal viability have been done on cornea with cells It seems that by "corneal viability" is meant "corneal cell viability" which is based solely on culture cell growth In a previous communication we urged a re examination of this concept(2) If the cells from the cornea can be removed and the remaining portions studied as to its properties, this question can be enlightened further This would be a step forward in the study of corneal grafting as well as in other branches of tissue transplantation where the non cellular structures are considered dead(8)

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transparency, slightly clearer than the three King s corneae (7) we have used and equally as good as the cellular lamellar human cornea (3)

In the unfavorable host group (Table 2) after initial transparency they survived with partial or total opacification depending on the extent of unfavorableness of the bed In two cases where the bed was cauterized with formalin for bleeding they took' but although

TABLE 2 — *Unfavorable Acellular Lamellar Homotransplants*

Age and Size of Graft	*Hours after death*	*Diagnosis*	*Results*
Fresh 7 × 5 mm	5 Hours	Keratitis Dendritic Recurrent OS	Transparency / / / / in 24 hours 4 days post-op Dehiscence noted Edema periphery Not fully epithelized Graft opaque a mo after surgery
4 Days 9 × 5 mm	12 Hours	Keratitis Vascularizing Koch OS	Transparency / / / / in 24 hours 2 days post-op Intralamellar bleeding Not absorbed w/corneal stain ing Epithelized in 5 days Good healing Removed on 19th pod for histology
40 Days 9 5 mm	15 Hours	Keratopathy Bullous Aphakia OS	Transparency / / / / in 24 hours Clearing up of edema in bed Epithelized in 7 days Good healing Slight edema after 2 mos Partially opaque in 6 mos Minimal deep B V
3 5 Mos 8 5 mm.	5 Hours	Corneal Ulcer Torpid OS	Transparency / / / / in 24 hours Epithelized in 7 days Edema of graft on 6th day Sutures removed on 14th day Graft detached and opaque the following day
7 5 Mos 9 5 mm	2 Hours	Leucoma Extensive Vascularized (Acid burns) OS	Transparency / / / / in 24 hours Good healing Epi thelized in 6 days Increase B V in bed Graft hazy on 17th day Under observa tions.

they survived morphologically for some time they gradually disinte grated like heterografts (Table 3) Whereas the cellular or acellular

in isolated corneas The embryonation conveniently removes the dead stroma cells It is by this means that we could obtain from the Philippine General Hospital Cornea Bank all the human acellular corneas that we have used in these clinical and experimental studies

Clinical properties of acellular cornea Human acellular corneal homograft We have used so far 24 human acellular corneas for lamellar grafting in various conditions of the host corneae These may be divided into those favorable without or very minimal vascularization for visual keratoplasty and those unfavorable with extensive leucoma, mostly adherent and vascularized or with active inflammation and/or infection for therapeutic, tectonic and cosmetic keratoplasty The graft used varied from those freshly taken from the cadaver to those stored in 95% glycerin for variable periods to as long as eight months These grafts have been followed from one month to almost a year now On the whole, in favorable host beds (Table 1), they survive with full

TABLE 1 — *Favorable Acellular Lamellar Homotransplants*

Age and Size of Graft	*Hours after death*	*Diagnosis*	*Results*
Fresh 9 × 5 mm	7 Hours	Keratitis Interstitial OS	Transparency //// in 24 hours Maintained Clearing up of edema in bed Minimal peripheral B V
10 Days 7 × 5 mm	5 Hours	Pterygium Extensive OD	Transparency / / in 24 hours Maintained Epithelized in 5 days Good healing Minimal B V from side of pterygium
21 Days 9 × 5 mm	10 Hours	Keratitis Superficial Recurrent Viral OS	Transparency //// in 24 hours Maintained Epithelized in 6 days Good healing Pathology arrested No Vascularization Granulation T
25 Days 9 × 5 mm	3 Hours	Keratitis *Disciform* OS (1 Mo old)	Transparency / / in 24 *hours* Maintained *Epithe*lized in 6 days Clearing up of aedema in bed Good healing Minimal peripheral B V
8 Mos 9 × 5 mm (Peritomy Partial)	5 Hours	Pterygium Extensive OD	Transparency //// in 24 hours Still clear up to present — 1 Mo after Epithelized in 8 days Good healing under observation

Table 4 — *Results of Acellular Heterotransplants*

Kind Size and Type of Graft	*Diagnosis*	*Results*
Fowl Ant Lamellar 7 mm Cosmetic	Leucoma Extensive Vascularized OD	Transparency / / / / in 24 hours Maintained up to 7th day Opaque in 25 days Gradually disintegrated and on 40th day only ½ of Graft left
Fowl Ant Lamellar 7 mm Cosmetic	Leucoma Extensive Vascularized OD	Transparency / / / / in 24 hours Maintained up to 5th day Completely opaque in 50th day Disintegrated and gone 2½ months after
Fowl Ant Lamellar 8 mm Cosmetic	Leucoma Extensive Vascularized OD	Transparency / / / in 24 hours Maintained up to 8th day Opaque in 45 days and gone on the 57th day
Fowl Penetrating 6 mm	Leucoma Extensive Vascularized OD	Transparency / / / / in 24 hours Persistent Posterior Edema Completely opaque on 14th day Gradual thinning and anterior bulge 48th day very thin Repeat keratoplasty

the Warburg apparatus for oxygen consumption The results are tabulated as follows [5]

Specimens	*Oxygen consumption* Co_2	*Results of Langham*
Whole Cornea Fresh (Chicken)	0 674 ml/hr/mg	0 864 ml/hr/mg
Cornea w out epithelium and endothelium Fresh	0 371 ml/hr/mg	0 230 ml/hr/mg
Stored whole cornea for 2 days in liquid paraffin	0 273 ml/hr/mg	
Acellular Cornea Fresh	0 214 ml/hr/mg	

heterografts (4) disintegrated after turning completely opaque these *homografts remained slightly transparent until they disintegrated* In one case where this acellular human cornea was used for penetrating therapeutic grafting, it survived morphologically but became opaque

Acellular chicken corneas were used in human eyes in four very unfavorable cases (Table 4) *for cosmetic and tectonic cases* The concept is that they would be less or not at all antigenic because it is

TABLE 3 — *Initially clear Acellular Lamellar Homografts that became partially opaque and disintegrated*

L M	Leucoma Extensive Vascularized OS (Post keratoplasty opacity)	Anterior Lamellar 9 × 5 mm OS Formalin 10% cautery of corneal bed 21 Days stored	Transparency / / / / in 24 hours Epithelized in 6 days Poor healing No *Vascularization* A mo after slight haziness, Then *gradual* disintegration from periphery Gone in *2 Mos*
D A	Leucoma Extensive Vascularized OD *(Post keratoplasty* opacity)	Anterior Lamellar 9 × 5 mm OD Formalin cautery 10% of corneal bed 10 Days stored	Transparency / / / in 24 hours Epithelized in 6 days Delayed healing, *No vascularization* of graft Edema periphery a month after and gradually disintegrated Gone in a month's time

believed that the corneal antigens come from the cells Although they survived morphologically for about two and a half months which was longer than the cellular *chicken heterografts, they eventually disintegrated* If the rejection were solely allergic in nature this in a way showed that the corneal antigens do not come entirely from the corneal cells It was observed that acellular homograft were less invaded by host blood vessels than the cellular graft

All these clinical characteristics of a cellular graft may be interpreted as those of biological survival or viability

Biochemical properties — Oxygen consumption Using whole fresh cellular cornea as control, acellular chicken corneas were tested by

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Acellular Cornea Fresh	0 214 ml/hr/mg	

These findings show that acellular cornea consumes some oxygen under room temperature in N S S It therefore respires although to a lesser extent than cellular cornea

Physiological Properties — Hydration and Dehydration Experiments These follow the technique and procedure of Harris experiments on hydration of human cornea All the corneal specimens were obtained from cadaver's eyes without enucleation For control and comparison we used acrylic plastic contact lens, gelfilm and formalinized cornea as well as fresh and stored cellular corneas Essentially the experiments consisted of weighing the specimens initially, after 2 hours in NSS at -/ 4°C and then after 3 hours in NSS at /-37°C The results are shown in Table 5

It will be noted that

1 Acrylic plastic contact lens did not show any change of weight
2 Gelfilm increased in weight at -/-4°C and more in / 37°C
3 Cellular cornea weighed a little more at -/ 4°C but much less at W37°C
4 Acellular cornea weighed more at W4°C but like the cellular cornea it could dehydrate and weighed less at / 37°C
5 When formalinized however, this property of hydration at -/ 4°C and dehydration at -/ 37°C decreased considerably but it was not completely lost

TABLE 5 — *Summary of Hydration Experiments on human corneas*

Specimens	*Initial Wgt*	*Wgt after 2 Hrs in NSS at / 4 C*	*Wgt after 3 Hrs in NSS at / 37 C*
Acrylic Plastic	20 9 mgs	20 9 mgs	20 9 mgs
Gelfilm	12 8 mgs	28 6 mgs	31 1 mgs
Cornea Cellular Fresh	127 5 mgs	128 8 mgs	120 1 mgs
Cornea Cellular Stored	136 2 mgs	137 8 mgs	109 3 mgs
Cornea, Acellular Fresh	129 2 mgs	151 3 mgs	131 8 mgs
Cornea Acellular Stored	105 2 mgs	127 0 mgs	101 9 mgs
Cornea Acellular Formalinized	91 3 mgs	85 3 mgs	87 1 mgs

Adapted after Harris Experiments

These experiments show that acellular cornea has the property of hydration and dehydration

Biological properties - Incorporation Studies

PROCEDURE

1 Left cornea of chicken frozen with Co_2 snow absolute alcohol mixture

2 250 microcuries of S35 as sodium sulfate injected subconjunctivally to each eye 48 hours later

3 Both corneas were removed 24 hours after injections

4 Unattached S35 removed by washing in several changes of water then fixed in 10% formalin

5 Radio activity determined quantitatively with scintillation detector and Geiger counter

RESULTS:

A	Scintillation Counter	
	Background	83 counts/min
	Count rate of S35 (324 micro curies)	42 counts/min
	Count rate of acellular cornea	Activity not high enough
	Count rate of cellular cornea	To be recorded by the detector Counts almost the same as background
B	Geiger Counter	
	Background	8 5 counts/min
	Count rate of S35 (324 micro curies)	27 counts/min
	Count rate of acellular	11 counts/min
	Count rate of cellular	9 8 counts/min

Remarks Acellular cornea also incorporates the radio isotopes In fact it even had a little higher concentration than the cellular cornea

AUTORADIOGRAPHY

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2 250 microcuries of S35 as sodium sulfate injected subconjunctivally to each eye 48 hours later

3 Both corneas removed 24 hours after injections

4 Unattached S35 removed by washing corneas, fixed in 10% formalin and prepared for histo pathology

5 Sections placed in glass slides and covered with radiographic stripping film (Kodak AR 10)

6 Preparations placed in light tight boxes

7 Film together with slide developed at intervals of 2 to 4 weeks and examined under microscope

RESULTS

Both cellular and acellular corneas show radio activity in the stroma layer as shown by an increase in the silver granules over the sections

Survival and growth of Descemet's membrane in the anterior chamber Descemet's membrane was obtained from cadaver and the endothelium was scrapped off It was laid on filter paper and measured in milli meters Then it was implanted into the anterior chamber of an absolute glaucomatous eye so that it had no contact with the host endothelium It was observed from time to time by slit lamp for transparency and morphological survival After three months it was removed from the anterior chamber, measured and histologically examined It was found that it survived morphologically, although it lost about 25% of its transparency But by measurement it had increased in size by a few millimeters This experiment shows that Descemet's membrane is alive and viable membrane and can survive and even grow without endothelium

The results of these experiments support observations in the clinics and histopathology In the presence of the endothelium, Descemet s membrane can increase in length, reduplicate and curl after surgery or traumatic injuries Thomas [9] mentions a histo pathological report from a case of marginal degeneration of the cornea where Descemet's membrane has thickened and increased three to four times the normal, in the absence of the endothelium It is also well known that Descemet s membrane in a descemetocele is elastic when viable but disintegrates when it becomes necrotic This shows that it can exist in two states, a living and viable state or a dead and necrotic state

At several instances, Hogan and Zimmerman [6] describe collagen fibers of the cornea in a dead and/or necrotic state, presupposing alive or viable state They mention that a degenerated structure is not in a dead state So when the corneal lamellae and membranes are described to be degenerated, it implies that they are not dead structures but can exist in a viable degenerated condition

SUMMARY

Acellular human and fowl corneal grafts were produced by instantaneous freezing to — 49 C and leaving them or embryonating them in chicken eggs for 48 hours For the first time acellular corneal grafts have been tried clinically in 26 lamellar and 2 penetrating keratoplasties The over all results show that when the host is favourable in lamellar keratoplasty the acellular homograft maintains its transparency to an extent equal or in some cases better than the frozen dehydrated cornea of the World Eye Bank Their transparent survival are similar to cellular graft When the bed of the host is unfavourable with vascularization anterior synechiae extensive leucoma or glaucoma they turn partially or totally opaque Four fowl acellular heterografts became totally opaque and disintegrated although their survival was longer than the cellular heterografts Two acellular lamellar homografts where the host beds were formalinized eventually disintegrated also

The acellular cornea was found by the Warburg apparatus to consume oxygen under *room temperature* in NSS although to a lesser extent than when the cells were present This shows some respiration of the non cellular portions of the cornea

It was shown that acellular cornea like cellular cornea has the property of hydration at /4 C and dehydration at /37 C This almost entirely disappears on soaking it in formalin Acrylic plastic lens and gelfilm could not dehydrate themselves at /37 C.

Incorporation studies have demonstrated that using S35 as sodium sulfate injected sub-conjunctivally *in vivo* that acellular cornea like the cellular can incorporate the radio-isotopes as shown by the Geiger counter and manifested radioactivity in the stroma layers as shown by autoradiography

Implantation of Descemet s membrane without endothelium into the anterior chamber demonstrated that it can survive morphologically with some loss of transparency but with slight increase in size after 3 months

Instances are cited from the literature where Descemet s membrane and stromal fibers can exist in a viable degenerated condition distinct from a dead or necrotic state

DISCUSSION

There is no definition of a living structure that is currently accepted by all because survival with life has been confused with propagation of life It seems that with reference to a particular structure survival and propagation can not mean the same thing If viability should mean the capability to survive with life then propagation or reproduction which is sometime used synonymously with growth is not a necessary condition in order that the structure should be viable In tissue culture it is observed that cells can survive with life but stop multiplying if some essential elements in the culture medium are lacking This is the concept of viability which we have followed in trying to answer the question are the non cellular portions of the cornea viable?

In the cornea barely 10% of the formed structure ' are cellular Hence if corneal viability should refer only to cellular viability almost 90% of its structures — membranes and fibers would be considered dead It seems therefore that corneal viability should refer not only to cellular but also to non cellular viability although reproduction which is merely one of life s processes may be possessed only by the cells

The concept that corneal viability is not essential to the maintenance of transparent survival in lamellar keratoplasty should be revised It should state that corneal cellular viability is not essential but corneal non cellular viability is necessary for successful lamellar keratoplasty It should also be made clear that the state of transparency is different from the maintenance of transparency While the basis of the state of transparency may be morphological physical biochemical and optical for both innert and living structures the maintenance of transparency is biological in the viable formed structures but not in those which are innert Hence if the biological processes are deficient the transparency of the viable non cellular portions of the cornea decreases or even disappears

May be keratoplasty is the first kind of tissue transplantation where acellular graft has been tried This may be followed in other

areas of tissue transplantation An acellular graft is another approach and a further step in the study of transplantation allergy Rejection of corneal homografts and heterografts should be differentiated from opacification with or without loss of viability and disintegration The phenomenon of viability has received very little attention in the understanding of the many events of corneal grafting It is time that viability should enter where allergy has heretofore been the sole consideration

CONCLUSION

There are sufficient clinical, pathological, biochemical, physiological and biological evidences that the non cellular formed structures of the cornea are viable in the sense that viability means the capability to "survive with life" with or without the property to "propagate life"

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TRANSPLANTATION OF CORNEA IN CHILDREN

BARKHASH S A (USSR)

Transplantation of cornea is an outstanding achievement of modern ophthalmology This remarkable operation however, is still rarely applied to children for fear of various complications related to their restlessness in the post-operative period Besides that, it is somewhat difficult to perform this operation on a child under general anaesthesia

We believe that this approach is incorrect It is precisely children that should be restored to normal vision as early as possible Besides that a few years' postponement of an operation will make it almost useless because the child will have developed grave amblyopia

Five hundred operations of corneal transplantation on children aged between 6 months and 15 years were made at the childrens department of the Filatov Institute

The transplantations were partial though nearly complete as well as those made layer by layer Sixty five percent of them were successful

Here are the basic prerequisites of an effective grafting operation on a child

1 Careful examination and pre-operative preparation of children
2 Proper selection of the surgical method.
3 Effective general anaesthesia
4 Prolongation of post anaesthetic sleep
5 Firm fixation of corneal grafts with a conjunctival band or corneal sutures
6 Use of tissue therapy and corticosteroids
7 Organisation of good care of children
8 Exercises to correct vision in amblyopic eyes

The following are the characteristics of the post-operative period milder symptoms of allergic reactions rarer occurrence of glaucoma and trophic disturbances stronger optic refraction

Our observations on corneal transplantation over the past 15 years prompt us to recommend its wider application to children with corneal opacities

GAMMA GLOBULINE, ENZIMES ET DIBAZOLE EN TRAITEMENT DE LA KERATITIS HERPETICA

N L MALANOVA

Med Ophthalmologiste, charge de cours, Clinique des Maladies Ophthalmologiques pres de l'Institut de Medecine de Gorki Directeur D M, *professeur B V Protopoov*

Jusqu'a present on n'a pas trouve les medecines capables d'action virus statique sur l agent de herpes cornea simplex C est pourquoi en therapie de la keratitis herpetica nous avons choisi la voie d'agir sur le systeme nerveux du malade compte tenu de proprietes neuro tropiques de l'agent A cet effet, nous avons administre le dibazole — sel chlorhydrique 2 benzile benzi midazole — qui est efficace lors des actions toxiques et infectieuses sur le systeme nerveux en remettant la sensibilite motrice, douloureuse et thermique apres troubles mecani ques du systeme nerveux, comme apres l'effet de poisons, d'agents microbiens et virulents

Dans nos experiments aux lapins, nous avons reussi de constater, que les injections prophylactiques du dibazole empechent l'origine et developpement de la keratitis herpetica experimentale

Injections du dibazole aux lapins exercaient une influence therapeutique evidente Les symptomes cliniques de la keratitis herpetica devenaient faibles et cessaient au 10–11 jour de maladie au lieu de 17–20 jour chez les lapins sous controle

Dibazole, ne s'exercant sur le virus de herpes, augmente la reaction et resistance d un macroorganisme par rapport a l agent seulement, c est pourquoi, il faut l'administrer en combinaison avec la therapie etiologique A cet effet, nous avons applique le gamma globuline *Son application est affirmee par le fait, que chez la majorite* de population adulte on trouve dans le sang un haut titre d anti corpuscules specifiques en regard a l agent de la keratitis herpetica Formation de ces anticorpuscules capables a neutraliser le virus, est liee avec l'existence de la fraction gamma globuline de protéines du serum de sang Concentration de ces anticorpuscules specifiques en series gamma globulines surpasse de 20–25 fois leur concentration dans le serum ordinaire de sang

Le traitement etait administre aux 60 malades aux formes diverses de keratitis herpetica Les 13 malades avaient la suffrance primaire les 17 — les recidives Dibazole était administré aux 8 malades in loco, sous forme d'une solution 1% par l electrophorese a l oeil, les

autres malades recevaient ce preparat per os — 0 02–0 03 trois fois par jour cette derniere methode de l application du preparat se trouva la plus efficace

Le gamma globuline était administre in loco, car justement dans le foyer de trouble nous cherchions de creer la concentration maximum d anticorpuscules Le gamma globuline etait instille dans l oeil souffrant 6–8 fois au cours de 24 houres ou on en injectait 0 5 ml sous la conjonctive de la sclerotique, plus près de la section troublee Ces injections etaient realisees chaque jour ou tous les deux jours en variant leur nombre total de 2 a 7 sous dependance de la gravite du procede

L administration du gamma globuline se trouve surtout efficace dans les cas frais ou il y a la phase virucemique de maladie Le mecanisme de penetration de la particule virulento dans la cellule n est pas etudie jusqu a present On sait, que la penetration du virus dans la cellule commense par adsorption des particules du virus a la surface de cellule Justement au cours de cette periode ci que les anticorpuscules commence a s exercer sur le virus Les anticorpuscules serums de reconvalescents se repartissent a la surface de cellules susceptibles en y empechant la penetration du virus

Chez malades dont la duree de souffrance ne surpassait pas trois semaine les sensations douloureuses dans l oeil et photophobie se baissaient au 2nd ou 3me jour du traitement administré Sensibilite de la cornee commençait a remettre les erosions herpetiques s epithe liaient

Dans les cas chroniques ou le virus s est deja localise endedans de la cellule l application du gamma globuline etait precedee soit par administration soit par instillation de la slution 1% tripsine, dans le sac conjonctival Tripsine comme possedant une action proteolytique donne lieu a destruction de proteines du virus, et alors il neutralise le virus en le preparant pour phagocytose Nous n avons constate aucun effet collateral du a l administration du tripsine, car nous ne l avons applique qu en concentrations faibles et combine obligatoirement avec l instillation du gamma globuline

L administration de preparats susmentionnes resultait en guerison des keratites herpeticae fraiches et chroniques aux troubles superficiels et profonds de la cornee

Chez malades aux troubles de la cornee chroniques, c est a dire hopitalises à cause de récidives de la keratitis herpotica, les procedes de reparation n etaient pas si complets les procedes inflammatoires etaient coupes sensibilite de la cornee remise vaisseaux de cornee superficiels et profonds devenant vides — disparus mais les changements cicatrisants de la cornée restaient et la remise du visus chez ces malades n était pas si complete que dans les cas frais

In 94 3% de cas il y avait une guerison complète dans 5, 7% il restait un stable trouble ds la cornee

En general, on sait, que les keratites herpeticae ont une forte tendance aux recidives En surveillant nos malades au cours de 1, 5-2, 5 annees, nous avons constate seulement un cas de recidive Il est evident, que dibazole en s'exerçant sur la transmission acetyle choline de l'impulsion nerveuse et se trouvant en correlation positive avec la cholinergie, stimule la resistance d'organisme contre le virus et y empeche les recidives possibles

PHYLOGENY IN HETEROGENEOUS KERATOPLASTY

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It has been suggested that opacification and vascularization of corneal grafts especially the heterografts are essentially dependent upon an antigen antibody reaction between the donor and recipient cornea (Babel and Bourquin 1952 Choyce 1952, Basu and Ormsby 1957) It has been pointed out that this donor recipient reaction is less marked the farther phylogenetically are the donor and the recipient (Basu and Ormsby 1957) It is also common knowledge that even autografts become opaque In all this assessment an important factor or hypersensitivity of the recipient has not been taken into account With a view to assess these factors the following aims were kept in mind by us

1 The relative antigenic properties of corneas of various species

2 The hypersensitivity of the host to the various antigenic corneas

3 The species specificity of corneal proteins,

4 Antigen antibody response to the antigens of corneas of various species,

5 The prediction of the end results of a corneal intralamellar graft on the basis of hypersensitive reaction and antigen antibody response

The above have been achieved by the following procedure

1 Experimental intralamellar grafting of cornea from various species into the rabbits eye

2 Response of human beings to corneal antigen from various species after intradermal injection

3 Electrophoretic studies of corneal antigen of various species

4 Agar gel diffusion study of antigen antibody response in rabbits after intraperitoneal injection of corneal antigen from various species

5 Intralamellar grafting in hypersensitive and insensitive rabbits and assessment of results

I EXPERIMENTAL RESULTS OF GRAFTING FROM VARIOUS SPECIES

A series of experiments were carried out in which rabbit was used as a recipient and the donor material was taken from four different phylogenetic groups, Pisces (fish), Amphibia (frog, Rana tigrina), Aves (chicken) and Mammalia (goat and dog) Ten grafts were performed with material from each species except dog from which only two grafts were obtained Full thickness 6 mm in diameter circular discs of donor cornea were grafted intra lamellarly by the technique of Agarwal et al (1962) in all the experiments One eye each from the first four series was enucleated one, two, four and eight weeks and three and six months after the graft and histopathological studies on them were done The rest were clinically observed

In this experimental study we observed that haziness of the graft occurring in the early postoperative period is mainly due to operative manipulations and was not associated with any ingrowth of blood vessels into the cornea In eyes in which donor recipient reaction occurred the opacification of the graft appeared after one week and was always associated with invasion of blood vessels into the host cornea which in severe cases progressed into the donor tissue In some eyes we observed that the reaction was quite intense in the host tissue which became markedly opaque, while the donor tissue was little affected and remained relatively transparent

This probably was a hypersensitive response of the host to the donor tissue in which the former showed an excessive reaction while the latter was little affected

This led us to believe that there are other factors besides the antigen antibody reaction which have profound influence upon the ultimate results of heterokeratoplasty

From our experimental studies (clinical and histological) we learnt that the frog heterograft aroused least reaction in the rabbit (Figs 1 and 2) followed by chicken (Figs 3 and 4) and fish (Figs 5 and 6) respectively The results were extremely poor in goat and dog series (Table 1 and Figs 7 and 8)

Our observations do not show exact correlation between phylogeny and opacification of the graft Frog and chicken are phylogenetically nearer to rabbit than the fish and the better results with these species do not support the views of Basu and Ormsby (1957) and go against the theory of phylogeny in the success of heterokeratoplasty

II RESPONSE OF HUMAN BEINGS TO INTRADERMAL INJECTION OF CORNEAL ANTIGEN

(a) *Preparation of the corneal extract*

The eyes were collected within 2-3 hours after the death of the animal and thoroughly washed with antibiotic solution Corneas were excised and made into fine paste by grinding with glass powder care being taken to keep the temperature as low as possible during the whole process to avoid denaturation of proteins An equal amount of

TABLE I — *End Results of Intralamellar Heterografts*

Series	No of grafts	Opacified +	++	Results +++	Extruded corneas	Clear corneas
Fish	10	4	5	1	1	—
Frog	10	—	—	—	—	10
Chicken	10	6	2	-	1	1
Goat	10	5	1	3	1	—
Dog	2	—	1	1	—	—

The results were read as follows

+ (One plus) When the opacity was slight and was seen with difficulty with the naked eye It was more obvious with slit lamp examination Iris and pupil was seen easily through the haziness

++ (Two plus) The opacity was moderately dense Iris and pupil was seen but details were not possible

+++ (Three plus) The opacity was dense and pupil and iris could not be seen through it

sterile normal saline was added and the whole thing was left for 48 hours at 4 C Centrifuging under refrigeration was done at 10 000 revolutions per minute for 15 minutes Clear supernatant fluid was dialyzed against distilled water to remove excess of salts The extract was concentrated by evaporation technique till the protein concentration rose to about 3% as determined by biurate method The extract was filtered through Seitz filter and its sterility was confirmed by negative culture

Corneal extract was prepared with the corneas of four species i e goat fish chick and frog

(b) *Intradermal test in human beings*

Intradermal tests were carried out in human beings by injecting the corneal extract of four different species mentioned above The extract was injected in the forearm skin so as to raise a wheal of about 4 mm size Normal Saline was injected as a control in the opposite forearm The reaction was read after 24 hours, 48 hours and 72 hours Table II)

These tests indicate that human beings show a varying degree of sensitivity to corneal antigens derived from various species The antigens from the frog cornea show the least response followed by chick fish and goat They do not show any correlation to phylogeny To 50 adult human beings of about 40-45 years of age in the right forearm intradermal injection of corneal antigen from all the four species was

TABLE II — *Intradermal test in Human beings*

Animal	*Total No of cases*	*Total No of cases showing + ve reaction*	*Degree of reaction*		
			+	++	+++
Goat	50	24	3	18	3
Fish	50	9	5	4	—
Chicken	50	8	5	3	—
Frog	50	3	2	1	—

Note

\+ Erythema more than 5 mm Induration less than 5 mm
++ Induration 5 to 8 mm
+++ Induration more than 8 mm

given A wheal of 4 mm was raised by the antigen of each species separately The wheal were separated from each other by an interval of two inches Similar four wheals were raised in the left forearm by intradermal injection of normal saline The results are given in (Table III)

TABLE III — *Response of human volunteers to various corneal antigens*

S No	*Number of cases (Total 50)*	*Frog*	*Fish*	*Chicken*	*Goat*
1	1	+	+	+	+
2	2	+	—	—	—
3	10	—	+		
4	2	+	—	+	—
5	2	—	+		
6	2	—	—		
7	2	—	+	+	
8	14	—	—		
9	15	—	—	—	

These results indicate that each individual is not sensitive to the antigens from all species This suggests to us that corneal antigen may be species specific and not organ specific This also gives an indication of probable choice of donor material

III ELECTROPHORESIS OF CORNEAL PROTEINS

Paper electrophoresis of the extracts from the cornea of different species was done on Whatman paper No I using barbitone buffer

ph 8 6 molar strength 0 1 at 150 volts for 18 hours Number of bands obtained and their percentages are given in table No IV and Fig 9

TABLE IV — *Electrophoretic patterns of corneal proteins from various species as compared to human serum*

	Albumin	*Globulin* %			
		Alpha 1 %	*Alpha 2* %	*beta* %	*gamma* %
Human Serum	57 39	3 86	8 50	13 75	16 50
Goat corneal extract	6 31	—	12 13	19 41	62 15
Fish corneal extract	—	—	22 34	27 10	50 56
Chicken corneal extract	40 28	—	—	35 15	24 57
Frog corneal extract	—	47 14	—	35 72	17 14

These bands and their relative percentages indicate that the nature of proteins of cornea of various species differs considerably These differences may be responsible for *species specificity* of these proteins The higher the gamma globulin percentage the more reaction it produces The content of gamma globulin *in frog's cornea* is very near the gamma globulin content of human serum This may be a factor accounting for its low antigenicity to human beings

IV ANTIGEN ANTIBODY RESPONSE TO THE CORNEA OF DIFFERENT SPECIES

Immune sera were obtained from rabbits after sensitizing them against the corneal extracts of above mentioned four species To achieve this intraperitoneal injections of corneal extracts were given twice weekly in increasing amounts (0 2 cc 0 2 cc 0 4 cc 0 8 cc 1 cc 1 0 cc 2 0 cc 2 00 cc) Three rabbits were sensitized against each species Quantitative estimation of antibodies was done by microprecipitation technique The positive titres were as follows

Goat 1 32 Fish 1 8 and Chick and Frog 1 4 (Fig 10)

The presence of antibodies was further demonstrated by agargel diffusion technique One per cent agargel was prepared in normal saline About 4 cc of this was put on a slide and allowed to set Bottom of the holes were sealed by gently warming the slide Antigen was

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2	2	+	—	—	—
3	10	—	+		+
4	2	+	—	+	—
5	2	—	+		+
6	2	—			—
7	2	—	+	+	
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put in the central hole and antisera in the peripheral holes The results are as in Table V

TABLE V — *Results of Agar gel diffusion technique of demonstration of antibodies*

Animal	*Number of bands Antigen and Immune serum*	*Control Antigen and Normal Serum*
Goat	3	nil
Fish	2	nil
Chicken	2	nil
Frog	2	nil

INTRADERMAL TESTS

With goat and frog corneal extracts intradermal tests were carried out in rabbits It was observed that in the goat series 8 out of 10 rabbits showed positive reaction In two rabbits the reaction was necrotising and in 5 it was +++ and in one it was ++ In frog series only three rabbits out of 8 showed positive reaction In 1 it was +++ in the remaining two it was ++ Keratoplasties were performed both on sensitive and insensitive rabbits

RESULTS

Frog series —Except for one (with +++ reaction) all other grafts remained transparent

Goat series —In all cases there was intense reaction resulting in opacification of the cornea Blood vessels could be seen in the host tissue towards the graft on the 6th and 7th postoperative day This vascularization persisted though its intensity started diminishing after 15-20 days The graft remained opaque in all these cases

These results indicate the possibility of an intradermal test as a means of predicting the fate of the graft, as well as the choice of the species The work is still in preliminary stage and has to go a long way before it can be established as a procedure It is being extended to the monkeys and the results will be awaited with considerable interest

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LAMELLAR KERATOPLASTY IN CORNEAL FISTULA

RAIS, HADI and YOUVITCHEVITCH (TUNISIA)

The fistula of the cornea is a characteristic affection in countries where TRACHOMA CONJUNCTIVITIS ASSOCIATE exist, particularly in Africa and Asia Only a tectonic Keratoplasty can spare the panophthalmia which is a major complication

But the presence of flattened camera aquosa is a difficult problem If the keratoplasty is considered as being the major indication for the treatment of the corneal fistula, the authors are not agreed for the technique employed We propose the lamellar keratoplasty as being the proceeding more indicated above all when there is a flattened camera aquosa We have treated by this technique thirty cases successfully

FUNCTIONAL DETERMINISM OF THE CORNEAL BIO ARCHITECTONICS IN PARTIAL KERATOPLASTY

MIHAI CARAPANCEA

However thoroughly the technical conditions of any of the numerous operative variants known to day in partial keratoplasty are observed, they yield quite unreliable results, even at the hand of the same surgeon ophthalmologist. Either the minute portion of the cornea remains definitely transparent or, after several days or several months, it becomes more or less cloudy or even opaque.

As all biological hypotheses regarding the failure of the operation have been invalidated, there is at present no criterion by which the maintenance of the transparency of the corneal transplant can be predicted.

The success of the implantation of a portion of tissue into a histologically similar tissue depends upon the rapid adaptation of the implant to the medium of the host tissue.

The rapidity of the adaptation is, however, conditioned, to a certain extent by the evolutive stage of the specialization of the respective tissue. It is well known that tissues, less developed in their specialization, adapt themselves more readily than those which are more highly developed, such as the cornea.

The cornea, a small skin fragment — the ectodermic derivation rendered transparent, is an evolutively differentiated tissue, as a consequence of local stresses determined by functional necessities of the visual apparatus.

In conditions of the slow adaptation of the corneal transplant to the new environment — host corneal medium, — the corneal graft retains for some time its unmodified biological personality as it cannot integrate itself into the neighbouring biological atmosphere. In the meantime irreversible regressive modifications with respect to the normal take place in the cellular functions of the transplant as it is expressed by the variable clouding of the corneal graft upto its complete *opacification*.

Thus, though two similar tissues with identical biologies have been brought into contact, — an actual in vivo culture being achieved, i.e. the survival in a live medium practically similar to that from which it originated — the biological harmony not taking place *in due time*, it has rendered priority appearance of irreversible

degenerative modifications in the cellular functions of the corneal transplant possible, as it is shown by the loss of transparency in the transplant (2)

In the long run the adaptation of the transplant to the new corneal environment takes however place, even in the imperfect conditions of complete opacification of the transplant since the corneal graft is not eliminated as a foreign body, as would happen in the case of a complete inadaptation of the transplant

My new explanation of the degree of opacification of the transplant and the corrective I consequently suggest are based on the principle of the adaptation of the corneal graft to the new medium of the host cornea in conditions of strict observance of the natural functional bio architectural structure of the cornea

The cornea is a transparent epithelio conjunctival membrane the cellular elements of which form six symmetrically disposed layers namely peripherally two epithelial layers of which the more important anterior one is placed on the layer of a fine basal membrane of its own then internally, two lamellar layers, and centrally the layer of its own cellular fibro elastic material which contains the lymphatic lacunar system

Thus the natural functional structure of the cornea consists in there six corneal lens layers — with their arrangement in the shape of spherical segments moulded over each other, in their arrangement of alternating thicknesses and in the alternating differences in certain layers in the thickness between center and periphery — are nothing but *the directed trabeculae of the biological lines of force* representing the expression of the organized materialization of the component cellular elements considered in their aggregate grouping

In fact *the cornea only represents the natural functional bio architectural systematization resulting from the organization of its cellular elements in conditions of existence of the determinism expressed under the aspect of two general structural patterns a bio mechanical pattern in corneal layers and a bio optical one in corneal lenses* (1)

The mechanical bio architecture of the corneal layers has the following characteristics

1 The convexity of one layer fills the corresponding concavity of the immediately anterior layer (Diagrams 1 2 and 3)

2 The layers include in the middle their own cellular material 90 of the entire corneal thickness) like a thick cemented pillar Diagram 3)

3 The thickness of the layers are disposed alternatingly balanced in the following way the anterior epithelium (layer 1) is by 3 60% thicker at the periphery than in the center, the basal membrane (layer 2) is by 0 15% thicker at the periphery than in the center the Bowman membrane (layer 3) is by 0 82% thicker in the center than

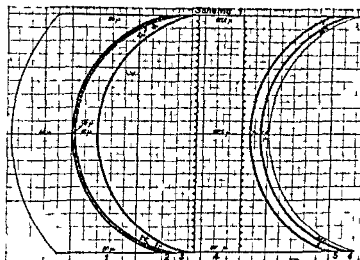


DIAGRAM 1 Diametral section of the cornea with the thickness of the component layers

1-6 Layers of the cornea

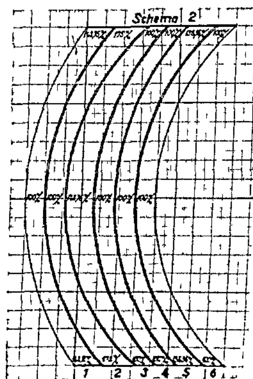


DIAGRAM 2 Diametral section of the cornea with the thickness differences of each layer in percentages to its own thickness

1-6 Layers of the cornea

at the periphery, while the Descemet membrane (layer 5), by 0, 32% thicker at the periphery than in the center, is comprised between two

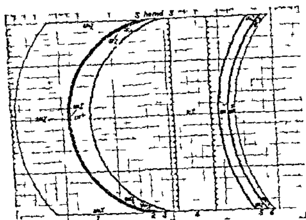


DIAGRAM 3 Diametral section of the cornea with the thickness of each layer in percentages to the total thickness of the cornea
1-6 Layers of the cornea

layers both identically thick over their entire extent in front its own cellular material (layer 4) represents 90% (layer 6) and behind the posterior epithelium 60% (layer 3)

4 The disposition of the thickness of layers and their orientation in their totality make out of the membrane — provided with a mechanical and statical function of enveloping and containing the anterior part of the eyeball — a more resistant architectural whole than if the cornea was a simple band made up of a single tissue of the same total thickness as that of the six component layers (Diagrams 1 2 and 3)

The optical bio architecture of the corneal lenses has the following characteristics

1 The corneal layers are transparent

2 The convex concave shape of the layers in their above described alternating thickness confers them the value of irregular convex concave lenses (layers 1 2 3 and 5) and of regular ones (layers 4 and 6) (Diagrams 1 2 and 3) the value is however only theoretical as the layers being histologically welded together, they practically form a convex concave dioptric system the corneal lens in the shape of a convergent meniscus thicker by 33 5 μ at the periphery than in the center (Diagram 1) in which refraction occurs at the level of the anterior surface of the anterior epithelium and of the posterior surface of the posterior epithelium

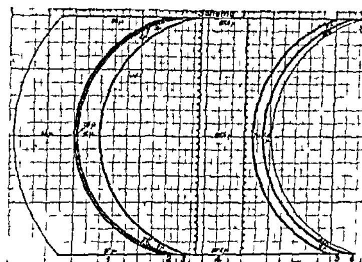


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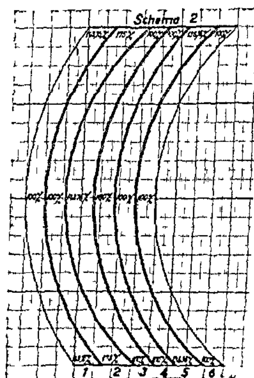


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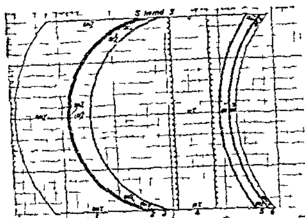


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The above facts show that the explanation of the situation of the opacified (leucomised) transplant must be looked for in the non observance by the graft of the host corneal bio architecture, in other words in the intercellular fusion of the layers if the two corneae which do not comply with normal histology, without observing the identity dualism of a corneal graft layer towards the same corresponding layer of the host cornea, thus not respecting either the local metabolism of the two corneae brought into contact with each other

The functional — anatomical realities of tissues in general are undoubtedly also based on the respective unquestionable local metabolisms which are however, still unknown to us in their immense complexity Particularly in the case of corneal metabolism, many anabolic and catabolic functions undoubtedly intervene, functions which are just as delicate as that fulfilled by this transparent film of the organ of vision

As the layers of the transplant do not correspond to the anatomical continuity of the surrounding corneal layers, not being in contact with one another, they will find themselves facing different layers each having its own physiology Hence the imperfect interaction of the functional anatomical relations between the biological processes of the two corneae brought into contact, and no harmonious whole in its general physiology will therefore be formed

The fact has generally been observed, without any explanation being given, that the transparency of the transplant is more often ensured if the leucoma is completely extirpated, down to the normal tissue, than if the transplant is placed into a leucomatous tissue In other words, it is obvious that the chances of maintaining the transparency of the transplant are greater if the bio architecture of the host cornea is at all observed On the other hand the *occasional* achievement of the histo architectural harmony between the layers of the two corneae explains the variable proportions of successful operations by the same surgeon

Partial keratoplasty, as practised to day puts two similar tissues into contact, but *by no means* two similar structures, so that the biological properties of the transplant layers will finally coincide only along general lines with those of the layers of the host cornea Hence it will result in a general adaptation of cornea to cornea but by no means a detailed adaptation of corneal layer to corneal layer In this case the viability of the new corneal entity will be ensured only in conditions of cloudiness resulting from low biological exchanges with the surrounding cornea at this level Thus, as the corneal lens layers of the transplant do not find similar histo functional correspondents in the neighbouring layers of the host cornea — i e they cannot adapt themselves to the corneal graft medium — a corresponding degree of reduction of the transplant transparency sets in, in proportion to the metabolic disturbances of the consequent development of the conjunctival tissue

The various degrees of cloudiness and opacification mean, therefore the expression of imperfect mutually harmonious relationships between transplant and the neighbouring cornea

The striking fact however is that, whatever the degree of its cloudiness the transplant should remain more or less independent and isolated retaining its biological personality even in the midst of the same material which it is made itself of The maintenance of its personality also depends undoubtedly to some extent upon the subsequent state of neurovegetative correlation — consisting of the regeneration of the nervous fibres — a very difficult process of anatomical restoration In this connection it is of interest to note that 17 days after transplantation the corneal graft presents a well defined sensitivity in its most peripheral portion (Jorn Boberg Ans), a situation which is in concordance with the general topography of the normal corneal sensitivity which presents a localisation all the more difficult as it approaches the central portion of the normal cornea

The biological aspect of the enclavement of the transplant should however also be considered from the point of view of the host cornea In other words a foreign normalizing state occurs in the region of the bed of the former leucoma in the place in which the host cornea was adapted to an abnormal state of its own One may therefore speak of a readaptation to normal conditions for the host cornea in the region of the extirpated leucoma and of a biological integration for the transplant

The structural reality of the cornea thus imposes the notion that since the layers of the cornea vary according to the region involved only the observance of the local bio architectural concordance between the two corneae in contact with each other can guarantee the perfect functional integration of the transplant into the host cornea in the sense that only the correct histological unification of the corresponding layers of the transplant and of the host cornea can guarantee the maintenance of the transparency of the transplant

The morpho functional bio architectural concordance between corneal graft and host cornea imply necessarily the following conditions

1 The transplant should have a topographical situation on the cornea from which it was taken identical with that of the leucoma in the cornea from which it was extirpated,

2 The orientation of the transplant should be identical at the site of the lack of material in the host cornea with that in the place from which it had been extirpated

3 The transplant should have an identical curvature with that of the host cornea which implies the same slope in the corresponding cellular planes as that of the peri transplantic layers

4 The transplant should have its cellular layers of an identical thickness as that of the corresponding ones of the host cornea which

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Partial keratoplasty, as practised to day puts two similar tissues into contact, but *by no means* two similar structures, so that the biological properties *of the transplant layers will finally coincide only* along general lines with those of the layers of the host cornea Hence it will result in a general adaptation of cornea to cornea but by no means a detailed *adaptation of corneal layer to corneal layer In this case* the viability of the new corneal entity will be ensured only in conditions of cloudiness resulting from low biological exchanges with the surrounding cornea at *this level Thus, as the corneal lens layers of the* transplant do not find similar histo functional correspondents in the neighbouring layers of the host cornea — i e they cannot adapt themselves to the corneal *graft medium — a corresponding degree of* reduction of the transplant transparency sets in in proportion to the metabolic disturbances of the consequent development of the conjunctival tissue

The various degrees of cloudiness and opacification mean, therefore the expression of imperfect mutually harmonious relationships between transplant and the neighbouring cornea

The striking fact however is that whatever the degree of its cloudiness the transplant should remain more or less independent and isolated retaining its biological personality even in the midst of the same material which it is made itself of The maintenance of its personality also depends undoubtedly, to some extent upon the subsequent state of neurovegetative correlation — consisting of the regeneration of the nervous fibres — a very difficult process of anatomical restoration In this connection it is of interest to note that 17 days after transplantation the corneal graft presents a well defined sensitivity in its most peripheral portion (Jórn Boberg Ans) a situation which is in concordance with the general topography of the normal corneal sensitivity, which presents a localisation all the more difficult as it approaches the central portion of the normal cornea

The biological aspect of the enclavement of the transplant should however also be considered from the point of view of the host cornea In other words a foreign normalizing state occurs in the region of the bed of the former leucoma in the place in which the host cornea was adapted to an abnormal state of its own One may therefore speak of a readaptation to normal conditions for the host cornea in the region of the extirpated leucoma and of a biological integration for the transplant

The structural reality of the cornea thus imposes the notion that since the layers of the cornea vary according to the region involved only the observance of the local bio architectural concordance *between* the two corneae in contact with each other can guarantee the *perfect functional* integration of the transplant into the host cornea in the sense that only the correct histological unification of the corresponding layers of the transplant and of the host cornea can guarantee the maintenance of the transparency of the transplant

The morpho functional bio architectural concordance between corneal graft and host cornea imply necessarily the following conditions

1 The transplant should have a topographical situation *on the cornea from* which it was taken identical with that of the leucoma in the cornea from which it was extirpated

2 The orientation of the transplant should be identical at the site of the lack of material in the host cornea with that in the place from which it had been extirpated

3 The *transplant should* have an identical curvature with that of the host cornea which implies the same slope in the corresponding cellular planes as that of the peri transplantic layers

4 The transplant should *have its* cellular layers of an identical thickness as that of the corresponding ones of the host cornea which

implies the same age of the transplant as that of the host cornea, and, at the same time, the bringing into contact of two similar biological forces

In partial non penetrating keratoplasty, the basal layer of the transplant should be, in conformity with normal histological alter nation, *immediately above the layer* constituting the bed of the host cornea Therefore the simple quantitative replacement of the leucoma by a transplant of the same thickness is inadequate, since in practice the thickness of the cloudy, infiltrated corneal layers, thickened by the conjunctival tissue of the leucoma, corresponds to a much smaller number of transparent corneal layers of the transplant,

5 The transplant should have as small a surface as possible in order to observe the configuration in depth of the layers of the host cornea, *since the more extensive it is, the less it will observe the configu* ration in depth of the layers of the host cornea

Practical Conclusion

The transplanted cornea should replace the leucoma in identical functional, structural conditions with those of the host cornea at the place of the extirpated leucoma, so that the local observance of the general dispositions of the biological lines of force materialized in *histo architectonically* organized trabeculae of the two corneae brought into contact, i e the inter corneal morpho functional bio architecture, should form a non differentiated and isorefringent vital *whole*

The Laboratory for Clinical and Experimental Eye Physiology of the Normal and Pathological Physiology Institute " Daniel Danielopolu " of the Academy of the Rumanian People's Republic Director of the Institute Academician Prof Dr Gr Benetato

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1950 *Archives d Ophtalmologie* X 1 p 51-57

ARTIFICIAL EPISCLERAL SCHLEMM S CANAL FOR JUVENILE CONGENITAL GLAUCOMA

Dr B L PANDE
Ophthalmic Surgeon, U H M Hospital *Kanpur* (*U P*)

The modern conception about the pathogenesis of juvenile and congenital glaucoma is a maldevelopment at the angle of the interior chamber mostly maldevelopment of the Schlemm s canal leading to defective drainage of the aqueous humour from the anterior chamber

Goniotomy Operation which is the operation of choice in such cases requires costly equipment like the goniscope etc to achieve ultimate success

The few cases of goniotomy or even those supplemented with Gonipuncture in juvenile and congenital glaucoma I have come across have not impressed me at all Perhaps Goniotomy is *not able* to correct the deficiencies and defects of Schlemm s canal *it can only* correct those defects which are limited to the angle of the chamber (Anterior) I have threfore adopted the following surgical procedure for these cases which have given good results in my hands

I take the conjunctival flap (Fig 1) along with the sub *conjunctival* tissue as in sclerocorneal trephining or iridencleisis *from* 3 *to* 9 o clock (upper half circumference of the limbus) and dissect it with the Lang s or Fooke knife as far forward over the cornea as possible Then I insert three episcleral silk sutures (Fig 2) at 12 o clock 10 *o clock and* 2 o clock as far forward as possible near the limbus making allowance



FIG 1



FIG 2

for the Keratome incision at the limbus *to open* the anterior chamber just in front of these sutures a keratome *incision* is made and enlarged with Castroviejo corneal scissors *to complete* the opening from 3 to 9 o clock

Then a big 8–10 mm or three small pieces of 3–4 mm elliptical piece of tarsus is or *are taken from* the patient's upper lid if it is healthy and nontrachomatous otherwise a big 8–10 mm or three small pieces of

implies the same age of the transplant as that of the host cornea, and, at the same time, the bringing into contact of two similar biological forces

In partial non penetrating keratoplasty, the basal layer of the transplant should be, in conformity with normal histological alter nation, immediately above the layer constituting the bed of the host cornea Therefore the simple quantitative replacement of the leucoma by a transplant of the same thickness is inadequate, since in practice the thickness of the cloudy, infiltrated corneal layers, thickened by the conjunctival tissue of the leucoma, corresponds to a much smaller number of transparent corneal layers of the transplant,

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Two cases will illustrate the points —(1) Mr Z a case of absolute glaucoma was operated in July 1957 for his right eye Tarsal plate from his own upper lid was grafted Before operation the right eye tension was 55 (Maclean s tonometer) After operation tension came down to 30 Maclean s which was again checked after 2 months in the first week of September and found to be the same

(2) Mrs R admitted on 28th July 57 discharged on 23rd August 57 Juvenile glaucoma of the left eye Tension 33 mm Hg before operation right eye ulcer cornea resulting from phlyctenular keratitis Cartilage from the left ear was grafted and tension came down to 15 after operation The patient did not come back for a check up of the progress obviously because there was no need the result of the operation having given her permanent relief

Supplementary Data for Artificial Episcleral Schlemm's Canal in Juvenile and Congenital Glaucoma

Further following four cases were selected for the experiment besides two already quoted

Due to anterior synechiae the angle was blocked in all cases almost alround the limbus which was not much disturbed simply to observe the effect of the operation (except in case of No 3 at the cyclodialysis operation alone) or in all cases whatever anterior synectomy happened to have been automatically done while making a limbal section They were all cases of absolute glaucoma but with intact ciliary body function

CASE NOTES

(3) P R S Secondary Glaucoma after Cataract Extraction

Angle of the anterior chamber was altogether blocked alround simulating juvenile glaucoma In 1959, Cyclodialysis (transcleral) was performed and tension remained controlled for one year In 1960 tension again shot up to 55 mm Hg Schietz and could not be controlled by repeating cyclodialysis Ultimately the artificial episcleral chlemm s canal was made and tension is all along controlled till now

(4) A S Absolute Glaucoma

Angle blocked all through in right eye by multiple anterior synechiae Admitted on 7th December 1960 operated on 13th December 1960 discharged on 24th December 1960 Tension before operation 60 mm Hg Schiotz Tension at the time of discharge 30 mm Hg Schiotz Tension one week after being discharged 23 mm Hg Schiotz

(5) Mrs S W Case of Aphakia Right Eye

Operated for traumatic cataract at the age of 9 years In 1959, at the age of about 35 years developed glaucoma in this eye and was trephined for the same on 10th December 1959 Tension persisted hence cyclodiathermy as performed on 6th January 1960 with no

3–4 mm piece of cartilage from the external ear is or are taken and fashioned to suit the curve of the limbus The width of the piece or pieces should be about 3 mm or so and the anterior concave side of the piece should be thinner than the posterior convex side

After turning the conjunctival flap over the cornea, the piece should be adjusted and fixed over the sclera at the site of the sutures by means of the latter which are brought above the piece in the centre of its width at these three places (12, 10 and 2 o'clock) As in (Fig 3) The sutures are not tied at this stage but are brought above the corneo conjunctival flap almost at the junction of conjunctiva with the cornea by entering the flap from underneath as in the case of the tarsal or cartilage plate and tied over there (Fig 4) The

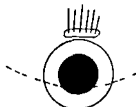


FIG 3

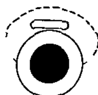


FIG 4

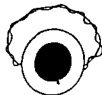


FIG 5

conjunctiva is sutured with continuous sutures (Fig 5) The usual dressing is done daily or on alternate days and the sutures removed after about a week

PRECAUTIONS

Before taking the sutures over the conjunctiva at the limbus from underneath, the flap of the latter should be stretched thoroughly well above towards the forehead so that (*i*) the sutures are fixed almost at the junction of the corneo conjunctiva and (*ii*) the plate keeps the anterior chamber slightly open by keeping away the cornea from coming in contact with the cut scleral margin

Advantages This operation requires very little or only cheap equipment as compared with the goniotomy operation and the results are much better and permanent

Disadvantages

(1) It is more time consuming and

(2) needs greater technical skill

NOTE Two narrow strips (each 1 mm wide) are cut out from the width of the plate at 11 o clock and 1 o clock after fixing the plate on the sclera by sutures it might prove a still better filtering channel and a genuine Schlemm s canal, though personally I have not yet tried it so far Two deep grooves at these two places in the plate made by a sharp cataract knife might serve the same purpose as taking out of the strips

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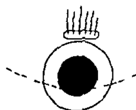


FIG 3

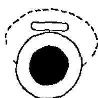


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PATHOGENIC TREATMENT OF GLAUCOMA

Prof KHAYUTIN S M (USSR)

Investigations which have been carried out for many years in the eye clinic of the Yaroslavce Medical Institute in the USSR have confirmed that glaucoma is the sequel of prolonged lesions of meta bolic processes in the eye These lesions may occur in consequence of injury of nervous elements of the eyeball optic nerve and central nervous system The first manifestations of these lesions appeared as patho logical fluctuations of intraocular tension The latter may be caused by local congenital and acquired alterations

The changes in the regulation of the intraocular tension may occur as a result of local and systemic disease or injury which influences the normal functioning of the nervous system anoxia in anaemias cardiovascular diseases and endocrinal disorders toxic action of products of metabolism in chronic gastro intestinal diseases diseases of liver and kidneys changes in the structure and function of the central nervous system due to trauma changes in the efficiency of brain cells due to permanent overworking or mental trauma etc

High prevalence rate of glaucoma in aged persons whose brain cells efficiency is rather often decreased occurrence of glaucoma in cases with mental trauma as well as the finding regarding the action of pentothal sodium aminatin novocaine etc confirmed the consi derable role of the functional capacity of the central nervous system in the regulation of intraocular tension

Our investigations of different degree of decrease of the intra ocular pressure in the eyes of the same glaucoma patient subject to barbiturates and neuroplegic drugs and to the stage of the disease and its compensation have shown the importance of local changes in the pathogenesis of glaucoma

Clinical and experimental investigations have shown that local effect of miotics and other drugs depends on the type and size of the lesions in the glaucomatous eye as well as on the functional capacity of the patients nervous and cardio vascular systems

Treatment of glaucoma should be aimed at the removal of the lesions which deteriorate the nervous activities in particular of the reflex arc regulating the intraocular tension The treatment should be aimed also at the improvement of metabolic processes in the eye to prevent further deterioration of the vision It may be achieved by the removal of unfavourable factors influencing the functional capacity of the nervous system. Besides the removal or decrease of the influence

effect All the above operations were performed outside as stated by the husband of the patient On March 2, 1961, I examined the case and tension was found to be 50 mm Hg Schiotz with no vision This operation was done on 24th March 1961 Right eye tension on 8th April '61 40 mm Hg

Pilocarpine and massage was prescribed on 8th May '61 Tension came down to 35 mm On 15th October '61 Tension was found to be *38 (patient stopped pilocarpine and massage since one month) On* 14th November 1961, tension was again felt and it was found reduced to 33° Advised to continue pilocarpine and massage

(6) H P Secondary Glaucoma with no vision in left eye

Angle blocked allround Tension 32 as given to me on 10th April '61 operated on *11th April '61 (taken at L L R Hospital)* and tension checked on 30th April, 1961 found to be 16 mm Hg Subsequently, the tension was checked again after two months, and was *found to be the same She had once been operated for glaucoma* for this eye some years back by some one else locally and had some vision before operation

The right eye was trephined by me in 1959 for chronic simple glaucoma and she is seeing with the same eye

Tension again checked on 19th November 1961 which remains as before

Note *If this operation is supplemented* with anterior synechotomy or transcorneal cyclodialysis (Pande —1956 A I O S Proceedings) it would give better results It *would be most beneficial* for cases like No 5 where the tension has not touched normal after operation though remains controlled

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at the factors like infections, autointoxication, alteration of oxidizing processes, etc , it is necessary to improve central nervous function in using suitable treatment programmes

It was found out in our clinic that intravenous and parorbital injection of novocaine improved the absorption of the tissue fluids, slightly decrease the blind spot usually enlarged in glaucoma patients and improve the nourishment of the retina Novocaine also strengthened the local action of the miotics

A special attention should be paid to the hemodynamics The changes of the vascular wall, contraction of arterioles and other vascular pathology gradually deteriorated the processes of metabolism In such cases, the treatment should be aimed at the decrease of abnormal blood pressure The attention of the ophthalmologist should be also paid to the cases with arterial hypotensions which may often lead to the decompensation of the glaucomatous processes in the patients with relatively mild intraocular hypertension

It is also necessary to keep in mind other signs of hemodynamics as intravenous tension, speed of the bloodstream, the data of ECG etc Because of the increase of the prothrombin index in many of glaucoma patients we have applied anticoagulants to facilitate the bloodstream, to prevent the thrombosis of venules and to improve the eye metabolism

The treatment of arteriosclerosis and gastro intestinal disorders, prescription of drugs to improve the barrier function of the liver, etc is also very important Endocrine therapy, properly applied, may have considerable influence on the course of the disease Sparing regime, vitamin rich diet, periodical taking of iodine and salicylate, mild sedatives and soporifics, oxygen and novocaine, while improving the general state of the patient may improve the condition of his eyes

Local treatment of glaucoma should include improvement of the blood circulation circulation of the aqueous humor, increase of oxidizing processes The local treatment should be combined with systemic treatment

Surgery should be recommended in early stage, in cases with congenital lesions or sequel of inflammatory or dystrophic processes causing narrowing or obliteration of the angle of anterior chamber and other changes disturbing due outflow of aqueous humor which cannot be improved by miotics and diamox

The operation should help to eliminate the causes of hindering the outflow of aqueous (goniosynechiae anterior and posterior synechiae, changes of the trabecular *net* of the angle of the anterior chamber and of the lens position, cataract etc) The surgery includes trabiculotomy, the operation performed in our clinic

The operation, the description of which, was *published* for the first time in June 1960, consists in the routine separation of the bulbar conjunctiva, incision of the sclera near the limbus and insertion of the

eye spatula or trabeculotome in the anterior chamber By rotating the trabeculotome along the chamber angle for a distance of 90–100 degrees the surgeon separates the trabeculae and destroys the existing goniosynechiae In case of shallow anterior chamber, narrow or closed by iris angle, partial or full pupillary block trabeculotomy has to be performed with external iridectomy

In late stages of glaucoma particularly in cases with rubeosis of iris thrombosis of the retinal vein as well as in cases of hypersecretion we perform the deep cyclodiathermy-coagulation Unlike the other methods of cyclodiathermy coagulation we try to avoid the coagulation at sclera because it may lead to its shrinkage and may favour the increase of intraocular tension

However these operations and the operations which help to form additional ways for outflow of aqueous and to improve the circulation of the aqueous, do not sufficiently normalise the metabolic processes The quantitative and qualitative composition of aqueous apparently is not sufficient for the eye tissue nutrition in the majority of the glaucoma patients who were operated This assumption is confirmed by the speeding up of cataract development and by further decrease of eye sight in spite of normalisation of the intraocular tension which is rather often observed after the performance of filtrating operations

The treatment of glaucoma patients should be continued in spite of the normalisation of the tension Local treatment with miotics, particularly with pilocarpine, which improves blood and lymph flow inside the eye treatment with mesaton vitamins iodine and other drugs is indicated in cases where the intraocular tension reached the normal level after the operation

Therapy should be changed according to the general condition of the patient and clinical course of glaucoma It should be taken into account that the ability of glaucoma patients to the adaptation of the environment is not sufficient The glaucoma patients therefore should be advised to stay in better climatic and environmental conditions

Dispensarisation of glaucoma patients in our country provides the opportunity to follow up of the patients after the operation and to restart the treatment of those whose visual function decreases again due to various unfavourable factors

TOXIC TETRAETHYLELEAD GLAUCOMA

Clinical and Experimental Data

Z M SKRIPNITSCHENKO

Scientific Experimental Research Institute for Eye Diseases and Tissue Therapy, acad V P Filatov, Odessa, Ukraine, U S S R

Director—acad N A Poutschkovskaja, Senior Scientific Collaborator, *Z M Skripnitschenko*

Studying the state of organ of vision in persons dealing with tetraethylelead and ethylgasoline we revealed a number of pathological changes Clinical manifestations of these changes were due to the affection of neurovascular apparatus of the eye

While carrying out prophylactic investigations of worker's eyes at the length of 5 years neither amaurosis or marked fall in visual acuity were recorded, and changes in peripheral boundaries of field of vision were absent as well

Studying the eye vessels we observed the dilatation vessels at choroidal vessels and limbus to be present in some persons in particular, in those staying for long terms at factories Separate vessels grew over the cornea and branched out from periphery into its superficial layers The diameter of vessels along their stretch was not equal Here and there their scanty dilatations could be seen Changes in the vessels of retina were revealed as well The contraction of the artery was a characteristic feature in case

In comparison healthy persons with those being in contact with tetraethylelead the tension in the central artery of retina was increased While measuring it by Bailliart its average made up 50 8 mm Hg, thus exceeding that of healthy persons (40 45 mm Hg)

In most persons under investigations the difference in tension of central artery of retina and inside the eye was great (20 0–45 0 Hg) According to Lauber (1936) this difference about 20 0 mm Hg is considered to be sufficient to secure normal blood supply of retina and optic nerve

Kushuk M E (1938) proved the difference in tension of 13 0 mm Hg not to affect blood circulation in the vessels of retina

The presence of regional hypertension in eye vessels and great difference of both pressures (of eye vessels and ophthalmotonus) can explain the fact that in case of high level of intra ocular tension the visual acuity does not decrease and the field of vision and other, structures of the eye do not suffer

The dilatation of angioscotoma is another proof of the presence of the affection of retinal vessels In some of the persons observed angios cotoma had the form of either a half moon or that of closed rings situated paracentrally, thus reminding typical Bjerrum scotomas

The dilatation of angioscotoma often was combined with the contraction of retinal vessels and increased intra ocular tension

While carrying out prophylactic observations the character of ophthalmotonus control was studied by Filatov Kalfa elastonometric method Intra ocular tension was taken by Maklakov's tonometer of different weights 5 0, 7 5 10 0, 15 0 gm The normal limit for ophthalmotonus was considered to be about 28 0 mm Hg while taking its measurement with tonometer with 10 0 gm weight

Controlled investigations of healthy persons revealed the threshold of eclastometric curve in norm to vary from 12 to 20 and very rarely to be equal to 22 mm Hg The level of ophthalmotonus was within 16 0 — 26 0 mm Hg The rise in curves varied from 7 to 12 0 and rarely it was defined as high as 6 0 or 13 0 mm Hg

All these elastometric curves had the form of ascending line, the break of curves was not noted The data obtained concerning the norm of elastometric curves conform to available data of other authors

In patients dealing with tetraethylelead and ethylgasoline the normal type of elastometric curves was observed High threshold of curves (above 22 0 mm Hg) the increased level of intra ocular tension (above 28 0 mm Hg), the break of curves and the change of their ascension were noted In most cases the ascension of curves was above 13 0 mm Hg thus determining the long type of curves

High threshold of elastometric curves, ascension of ophthalmo tonus level and long type of curves are characteristic for the clinic of primary glaucoma Changes in elastometric curve reflected the inhibiting character of the process that developed under the influence of tetraethylead in the neuroreflectory apparatus controlling ophthal motonus Changes on the part of the eye conform to the data of general pathology thus determining the clinical picture of tetraethylelead affection It is characterised by the development of inhibiting process in central bounderies of nervous system

Persons with pathological types of elastometric curves were investigated in in patient department where the character of ophthal motonus was determined by means of a dynamic method of its investi gations by Maslenikov A I

Still in 1904–1905 Maslenikov was the first to propose to investi gate ophthalmotonus in the morning and in the night According to these investigations diurnal fluctuations of ophthalmotonus in healthy persons did not exceed 4 0 mm Hg

While investigating persons dealing with tetraethylead a part of them revealed diurnal fluctuations to be increased dimensions of these fluctuations depending on the level of ophthalmotonus This can be seen on the presented table

TOXIC TETRAETHYLELEAD GLAUCOMA

Clinical and Experimental Data

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Studying the state of organ of vision in persons dealing with tetraethylelead and ethylgasoline we revealed a number of pathological changes. Clinical manifestations of these changes were due to the affection of neurovascular apparatus of the eye.

While carrying out prophylactic investigations of workers eyes at the length of 5 years neither amaurosis or marked fall in visual acuity were recorded, and changes in peripheral boundaries of field of vision were absent as well.

Studying the eye vessels we observed the dilatation vessels at choroidal vessels and limbus to be present in some persons in particular, in those staying for long terms at factories. Separate vessels grew over the cornea and branched out from periphery into its superficial layers. The diameter of vessels along their stretch was not equal. Here and there their scanty dilatations could be seen. Changes in the vessels of retina were revealed as well. The contraction of the artery was a characteristic feature in case.

In comparison healthy persons with those being in contact with tetraethylelead the tension in the central artery of retina was increased. While measuring it by Bailliart its average made up 50.8 mm Hg, thus exceeding that of healthy persons (40–45 mm Hg).

In most persons under investigations the difference in tension of central artery of retina and inside the eye was great (20.0–45.0 Hg). According to Lauber (1936) this difference about 20.0 mm Hg is considered to be sufficient to secure normal blood supply of retina and optic nerve.

Kushuk M. E. (1938) proved the difference in tension of 13.0 mm Hg not to affect blood circulation in the vessels of retina.

The presence of regional hypertension in eye vessels and great difference of both pressures (of eye vessels and ophthalmotonus) can explain the fact that in case of high level of intra ocular tension the visual acuity does not decrease and the field of vision and other structures of the eye do not suffer.

The dilatation of angioscotoma is another proof of the presence of the affection of retinal vessels In some of the persons observed, angioscotoma had the form of either a half moon or that of closed rings situated paracentrally, thus reminding typical Bjerrum scotomas

The dilatation of angioscotoma often was combined with the contraction of retinal vessels and increased intra-ocular tension

While carrying out prophylactic observations the character of ophthalmotonus control was studied by Filatov Kalfa elastonometric method Intra ocular tension was taken by Maklakov's tonometer of different weights 5 0 7 5 10 0, 15 0 gm. The normal limit for ophthalmotonus was considered to be about 28 0 mm Hg while taking its measurement with tonometer with 10 0 gm weight

Controlled investigations of healthy persons revealed the threshold of eclastometric curve in norm to vary from 12 to 20 and very rarely to be equal to 22 mm Hg The level of ophthalmotonus was within 16 0 — 26 0 mm Hg The rise in curves varied from 7 to 12 0 and rarely it was defined as high as 6 0 or 13 0 mm Hg

All these elastometric curves had the form of ascending line, the break of curves was not noted The data obtained concerning the norm of elastometric curves conform to available data of other authors

In patients dealing with tetraethylelead and ethylgasoline the normal type of elastometric curves was observed High threshold of curves (above 22 0 mm Hg) the increased level of intra-ocular tension (above 28 0 mm Hg) the break of curves and the change of their ascension were noted In most cases the ascension of curves was above 13 0 mm Hg, thus determining the long type of curves

High threshold of elastometric curves ascension of ophthalmotonus level and long type of curves are characteristic for the clinic of primary glaucoma Changes in elastometric curve reflected the inhibiting character of the process that developed under the influence of tetraethylead in the neuroreflectory apparatus controlling ophthalmotonus Changes on the part of the eye conform to the data of general pathology thus *determining* the clinical picture of tetraethylelead affection It is charactensed by the development of inhibiting process in central boundenes of nervous system

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While investigating persons dealing with tetraethylead a part of them revealed diurnal fluctuations to be increased dimensions of these fluctuations depending on the level of ophthalmotonus This can be seen on the presented table

TABLE — *The level of Ophthalmotonus and its diurnal Fluctuations in mm Hg*

Level of Ophthalmotonus	*No*		*Diurnal Fluctuations*							
	Persons	*Eyes*	*Norm to 4,0 mm*	5 0	6,0	7,0	8 0	9 0	10,0	*Higher*
36 0-40 and higher	16	32	3	—	4	4	3	4	2	12
31 0-35 0	46	92	14	12	20	12	10	11	4	9
29 0-30 0	26	52	29	4	11	4	2	—	2	—
27 0-28 0	20	40	28	6	5	—	1	—	—	—
to 27 0	22	44	2	2	1					

Increased ophthalmotonus caused increased dimensions of diurnal fluctuations, regular rhythm of these fluctuations being disturbed as well The changing of the increase and decrease in ophthalmotonus was taking place irregularly at various diurnal time and unequal in both eyes Such unbalanced state of ophthalmotonus was determined by the development of neurosis in the apparatus controlling ophthalmotonus, this being characteristic of the clinical picture of affection by tetraethylelead as well

Changes in the organ of vision conformed to other signs of affection by tetraethylelead In contradistinction to inorganic lead investigated persons revealed no impairment in peripheral blood as well as no increased lead contents in urine

Changing in gastric juice acidity and in normal type of glycemic curve were characteristic of them

On the basis of electrocardiogram data changing in conductive cardiac system were determined that was clinically manifested by either bradycardia or by *tachycardia* combined with arrhythmia

The data obtained on the part of general state of the body testify the changes in the organ of vision to be only partial manifestation of general affection of the body by tetraethylelead

Stated toxic glaucoma appeared to be only some addition to the clinical picture of general affection by tetraethylelead The data obtained confirmed once more the presence of close connection and dependence of the eye on the body as a whole

Observations on animals were carried out to answer a number of questions concerning pathogenesis of toxic glaucoma For this purpose a method of gradual and lasting intoxication of animals by tetraethylelead was elaborated

In the period of acute intoxication by tetraethylelead some animals lost weight some revealed growing bald, permeability of vessels was sharply impaired extensive haemorrhages appeared convulsion attacks developed in which case opthalmotonus control was sharply upset Its increased level before the attack changed after it by sharp fall, sometimes below the norm.

In case of chronic intoxication of animals by tetraethylelead cholinesterase activity of blood serum decreased The character of ophthalmotonus control was determined by pathological changes of elastometric curves increased fluctuations of ophthalmotonus level, and its frequent increase above the stated norm In separate animals the upset in ophthalmotonus control was kept under observation at the length of 1–2 years, thus determining chronic character of affection

In contradistinction to healthy animals in rabbits subjected to tetraethylelead effect under the influence of adrenaline atropine, and pilocorpine elastometric curves of pathological types were frequently noted fluctuations being increased and ophthalmotonus reaching high level

Provocative investigations by pressing on the eye ball with the weight of 50 0 gr also confirmed pathological character of ophthal motonus apparatus in animals subjected to the effect of tetraethylelead

With the help of nephelometric method by Francheschetti and Willand the increase in protein contents in aqueous humour of animals subjected to tetraethylelead effect was stated to be increased Increased permeability of eye membranes was determined as well in compression tonometric investigations by Vurhaft M B when after pressing on the eye with 15 0 ophthalmotonus decreased considerably and segment volume of tonometric flattening of the cornea reached large dimensions Lasting period of hypotony supervening the compression of the eye pointed out to simultaneous decreased aqueous humour metabolism

Lasting hypertension in case of small segment volume of tono metric flattening of the cornea as well as small decrease in ophthal motonus pointed out to tetraethylelead to be able to inhibit the process of aqueous humour formation

Tetraethylelead influence on the ophthalmotonus control and development of toxic glaucoma can be explained by such complicated character of its influence

One more stated form of glaucoma of known aetiologic factors, the production of this disease on animal models the studying of a number of questions concerning the pathogenesis of its development can help to work out prophylactic measures for preventing the develop ment of this disease

The studying of toxic glaucoma can be of great use for elucidating a number of questions concerning the pathogenesis of glaucoma being a basic disease resulting in blindness

SCLERAL RIGIDITY IN MANAGEMENT OF OPEN ANGLE GLAUCOMA PATIENTS WITH MYOPIA

With Special Reference to Chinese Scleral Rigidity

PEI-FEI LEE, M D

The scleral rigidity in patients with high myopia is often reported to be somewhat lower than that of the normal eye The determination of coefficient of scleral rigidity is therefore desirable in the evaluation of intra ocular pressure when suspicion of early glaucoma with high myopic condition has arisen This fact and uncertainty in interpreting the myopic disc appearance and visual field abnormalities make the early diagnosis of glaucoma especially difficult The importance of early recognition of glaucoma in management of high myopic has been repeatedly emphasized by other investigators 1-3, 6-9, 11-14

The method of Friedenwald for clinical estimation of ocular rigidity by means of repeated paired tonometric readings has been reevaluated by Kronfeld and apparently has worked reasonably well and is useful for clinical purposes (4) It is true that the Goldmann applanation tonometer is superior than the Schiotz impression tonometer in estimating scleral rigidity but the impression tonometer of Schiotz is more convenient than the applanation tonometer, (6), (9) and the method of Friedenwald can be used for clinical purposes, when the applanation tonometer is not available

It is the purpose of this study to determine how important the scleral rigidity is in the management of high myopic patients who may have early glaucoma, and to report the estimated value of coefficient of scleral rigidity in normal eyes among a Chinese population

METHOD AND MATERIAL

Friedenwald's method of estimating scleral rigidity by means of repeated paired tonometric readings has been used in this investigation All measurements were made by the author with a certified Schiotz tonometer of American manufacture, during the hours from 8 30 to 12 30 A M and 2 30 to 6 00 P M with the patient in recumbent

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A portion of this paper was presented before the Third Joint Meeting of the Ophthalmological Society of the Republic of China and the Section on Ophthalmology Formosan Medical Association on Nov 25 1962 Taipei Taiwan and published in the Chinese M J 9 261 (Dec) 1962

position Applications of the tonometer of two to three seconds' duration were made and the oscillations of the pointer were carefully observed The whole or half scale unite closest to the average position of the pointer during the application was recorded as the reading The application were made first to the left and then to the right eye first with the lower weight and then with the higher weight Thus the sequence was Left 5 5 right 5 5, left 10, right 10, and so forth Because most people are more sensitive about their right eye and the position of examiner is on the right hand side of the patient the left eye was measured first in this series For the purpose of avoiding immediate cardiac reflex and thus reducing technical error the tonometer was always held covering the visual line of the examined eye for two to three seconds prior to applying the tonometer on cornea Every patient received at least two pairs of measurements per clinic visit and most of them had two clinic visits Data were then added together and divided by times of measurements as the actual value Coefficient of scleral rigidity was expressed according to the tables of Moses and Becker (6)

Tonography was practiced according to the method of Grant and tracings were made on an Esterline Angus recording unit with improved model MC Electronic Tonometer (V Mueller & Co) Intraocular pressure and facility of outflow (C) were calculated from the 1955 Calibration of the Committee on Standardization of Tonometers (AAOO) Gonioscopy was done with Koeppe s lens Barkan illuminator and Haag Streit binocular handmicroscope The tabular method of Moses and Becker (6) using the following formula for the correct C value in eyes with abnormal scleral rigidity was applied in this investigation

$$C = \frac{0\ 0215\ \Delta V_g + (E - 0\ 0215)\ \Delta V_c}{4E\ (Pt_{av} - Po_{corr} - 1\ 25)}$$

in which

- C is the coefficient of facility of outflow (Cu mm./min / mm Hg)
- ΔV_g is the change in ocular volume
- E is the coefficient of scleral rigidity as determined clinically
- ΔV_c is the change in corneal indentation volume during tonography
- Pt_{av} is the average of initial and final intraocular pressure during to tonography
- Po is the intraocular pressure of the undisturbed eye as estimated from scleral rigidity measurements with the Schiotz tonometer

The tonometric measurements reported herein were made on 570 normal and myopic eyes and on 29 myopic eyes associated with primary open angle glaucoma selected from the Eye Clinic National

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- C is the coefficient of facility of outflow (Cu mm./min / *mm Hg*)
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- Po_{corr} is the intraocular pressure of the undisturbed eye as estimated from scleral rigidity measurements with the Schiotz tonometer

The tonometric measurements reported herein were made on 570 normal and myopic eyes and on 29 myopic eyes associated with primary open angle glaucoma selected from the Eye Clinic National

Taiwan University Hospital. The basis for selection was compliance with the requirements of:

1. Having unilateral myopia.
2. Of being myopic and having received cycloplegic refraction.
3. Of having no specific ocular pathology nor refractive error.
4. Of being well relaxed, cooperative during the measurements, and with no history of glaucoma, and
5. Myopic eyes associated with primary open angle glaucoma.

For the convenience of comparison the myopia patients were divided into the following four groups:

1. Mild myopia (less than — 3 D)
2. Moderate myopia (— 3 D to less than — 6 D)
3. High myopia (— 6 D to less than — 10 D) and
4. Excessive myopia (— 10 D and over).[5]

RESULTS

I. NORMAL EYE

A total of 570 emmetropic, myopic and unilateral myopic eyes were investigated and the findings are shown in the table below.

TABLE I — *Shows the average value of coefficient of scleral rigidity in normal and myopic eyes*

Eye Condition		*Number of Eyes*	*Average F value*
Normal		236	0.0205
Myopia	mild	54	0.0212
	moderate	82	0.0202
	high	38	0.0194
	excessive	100	0.0167
Unilateral myopia			
Mild	normal	15	0.0209
	myopic	15	0.0207
Excessive	normal	15	0.0211
	myopic	15	0.0123

EMMETROPIC EYES

In 236 normal eyes, the mean value of coefficient of scleral rigidity (F) was 0.0205. Elder the age, higher the F was noticed in this series

Correlation coefficient between age and E is highly significant ($r = 0.22 > 0.181$ when $\alpha = 0.01$) (Fig 1 — A and B)

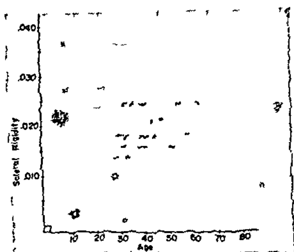


Fig 1 A Relation of age to scleral rigidity The frequency distribution of varying degree of scleral rigidity in 230 normal eyes is shown Greater the value of rigidity the older the age of the patient Most abnormally high rigidity was observed in the older age group

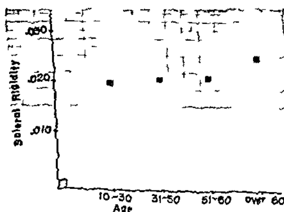


Fig 1 B Relation of age to scleral rigidity in 30 normal eyes in each of the four age groups Elder the age higher the rigidity is indicated Correlation coefficient between age and E is highly significant ($r = 0.22 > 0.181$ when $\alpha = 0.01$)

MYOPIC EYES

In 274 myopic eyes, the mean value of E varies according to the degree of myopia Higher the myopia, lower the E was observed It is also true in case of unilateral myopia (Fig 2— A and B) The differ

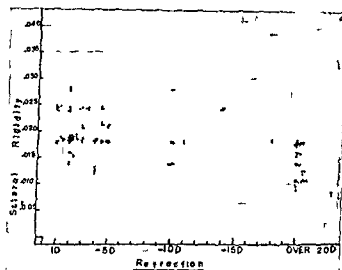


Fig 2 A Relation of myopia to scleral rigidity The frequency distribution of varying degree of scleral rigidity in 274 myopic eyes Lower than average normal value of rigidity is shown in the excessive myopia group

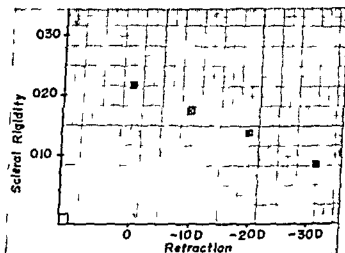


Fig 2 B Relation of scleral rigidity to axial refraction This figure indicates the higher the degree of myopia the lower the average value of rigidity *Highly significant difference of the E value between 51 mild and 100 excessive myopia* eyes is observed

$$\left(\frac{M_1 - M_2}{\sqrt{m_1^2 + m^2}} - 3\ 2 > 3\right)$$

ence of the E value between 236 normal and 54 mild myopia eyes was not significant but highly significant in normal and 100 excessive myopia eyes $\left(\frac{M_1 - M^2}{\sqrt{m_1^2 + m^2}} = 4\ 7 > 3\right)$ and also in 54 mild and 100 excessive myopia eyes $\left(\frac{M_1 - M_2}{\sqrt{m_1 + m_2}} = 3\ 2 > 3\right)$

For mild unilateral myopic cases, the mean of the differences of the E values between 15 normal and mild myopic eyes (Difference = E value of normal eye — myopia) has a 95% confidence interval of 0 0039 — 0 019 For 15 normal and excessive myopic eyes the corresponding mean has a 99% confidence interval of 0 0108 — 0 0026 Therefore, for excessive unilateral myopia cases, it can be concluded that the normal has higher rigidity than the myopic eye, but for the mild unilateral myopic cases the same conclusion cannot be drawn

TONOGRAPHIC AND GONIOSCOPIC FINDINGS

1 Excessive myopia Eleven of sixty excessive myopia cases received tonography and gonioscopic examination Two of these eleven cases showed slightly low outflow facility However this poor outflow facility apparently was due to the low E value rather than pathologically increased outflow resistance These C values were well within normal range after scleral rigidity correction (Fig 3 — A and B) Chamber angles were wide open and with no pathological finding gonioscopically in this group

2 Unilateral myopia Tonography and gonioscopy were performed in five of the 15 cases with unilateral mild myopia and 15 with unilateral excessive myopia The contralateral eye was normal and

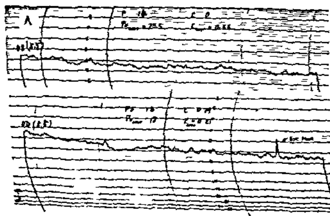


FIG 3 A Tonography tracings from an unilateral excessive myopia patient. Upper curve shows decline in myopia eye lower curve shows a normal C value in contralateral (normal) eye E and Po corrections are also indicated

MYOPIC EYES

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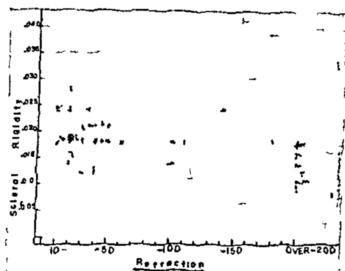


Fig 2 A Relation of myopia to scleral rigidity. The frequency distribution of varying degree of scleral rigidity in 274 myopic eyes. Lower than average normal value of rigidity is shown in the excessive myopia group.

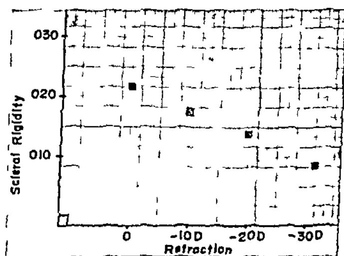


Fig 2 B Relation of scleral rigidity to axial refraction. This figure indicates the higher the degree of myopia the lower the average value of rigidity. Highly significant difference of the E value between 54 mild and 100 excessive myopia eyes is observed

$$\left(\frac{M_1 - M_2}{\sqrt{m_1^2 + m^2}} = 3.2 > 3\right)$$

TABLE II — *Coefficient of scleral rigidity in 15 unilateral excessive myopics*

Case No	Age	Sex	Tonomet Reading (R)		C — Value				Ref Index
			Eyes	R5 5/R10 0 Gm	E	Po corr	Before E Correction	After E Correction	
1	33	F	O D	5 25/ 9 5	0 0294	13 5	0 24		Em
			O S	6 25/11 75	0 0139	19	0 20		—22 D
2	53	F	O D	6 /11 75	0 0163	15 5	0 27		—23 D
			O S	5 / 9 25	0 0294	14	0 30		Em
3	11	M	O D	8 /14 5	0 0087	18	0 26		—20 D
			O S	7 /12 75	0 0124	17	0 27		Em
4	57	F	O D	4 5/11	0 0076	27	0 10	0 28	—25 D
			O S	4 5/9 5	0 0180	21	0 22		Em
5	26	F	O D	5 /11	0 0104	24	0 20	0 30	—12 D
			O S	4 5/8 75	0 0?95	16	0 26		Em
6	63	F	O D	5 5/10 5	0 0182	18	0 19		Em
			O S	6 25/13	0 0096	20 5	0 11	0 22	—18 D
7	37	F	O D	4 /9	0 0172	22	0 11*		—20 D
			O S	4 /9	0 0172	22	0 27		Em
8	42	F	O D	6 /11 5	0 0128	20	0 26		—17 D
			O S	4 5/9	0 0180	21	0 26		Em
9	61	M	O D	6 /12	0 0107	21	0 31		—25 D
			O S	4 5/9 5	0 0?13	18 5	0 29		Em
10	47	M	O D	7 /12 5	0 0139	16	0 23		Em
			O S	9 /15 5	0 0098	15	0 ?0		—16 D
11	41	M	O D	5 /10	0 0182	19	0 32		Em
			O S	6 /12	0 0107	21	0 23		—12 D
12	49	F	O D	7 /11 5	0 0237	11	0 26		Em
			O S	7 25/14	0 0078	20	0 21		—16 D
13	29	M	O D	6 5/12 5	0 0109	19	0 22		Em.
			O S	7 5/14	0 0086	19	0 14	0 19	—11 D
14	53	M	O D	7 /12	0 0179	14	0 23		—12 D
			O S	6 /10 5	0 0243	13	0 27		Em
15	18	F	O D	6 5 12	0 0139	17	0 24		—10 D
			O S	5 75/11	0 0159	18	0 26		Em
Average			Em.	5 47/10 40	0 0211	17 13	0 257		Em
			Myopia	6 37/12 33	0 0129	19 53	0 204		—17 25 D

* Borderline diurnal variation in IOP and positive water drinking test were also observed in this case.

Correction for C — value was made only in eyes which were more suspicious

a

b

c

d

FIG 3 B Tonography tracings from a bilateral excessive myopia patient who received the therapeutic pilocarpine test in O D Control eye O S Upper curves (a b) show apparently low *C* value O U especially in O D prior to pilocarpine test Lower curves (c d) showed *C* value *Po* and *F* were essentially uneffected by pilocarpine medication in O D There is essentially no change in control eye *C* value and *Po* corrections also indicated

with no refractive error in all cases Outflow facility appeared low in four of 15 excessive myopic eyes, but outflow facility in three of these four cases was well within the normal range after *F* correction Early open angle glaucoma was suspected in the remaining one case The *F* value of the two eyes was identical in this individual (Case 7) (Table II)

Chamber angles were wide open in all cases of unilateral myopia and showed no angle pathology gonioscopically

T s III Coeffic t f leral rig d'y p v or ted th p na p gl gl

Case No	Ag	S	T t R ad g R: Ey s	R5 5 R10 0	E	J o r	C alu: B f L Co ct	Af r F Correct	R fr ct Ind	Re n ks
1	60	M	O D	6 0 1	0107	21	0 07	0 11	— 17 D	L G 1
			O S	3 0 9	0088	31	0 03	0 09	— 15 D	
2	51	M	O D	4 5 10 5	0199	9	0 14		— 1 2 D +	
			O S	4 10	0197	32	0 08		— 1 25 D +	
3	38	M	O D	2 5/ 7	0238	26	0 10		— 3 5 D	
			O S	4 5/ 9 5	0217	19 5	0 16		— 4 5 D	
4	25	M	O D	3 0/ 8	0173	6	0 15		— 4 D	
			O S	? 0/ 8	0176	44	0 11		— 4 5 D +	
5	35	M	O D	5 0/ 9 5	0 46	16	0 11		— 2 D	
			O S	5 0/ 9 5	0246	16	0 13		— 0 5 D	
6	?4	M	O D	4 5/ 9 5	0180	21	0 10		— 1 5 D	
			O S	5 0/10	0182	19	0 12		— 3 D	
7	32	M	O D	3 5/ 9 5	0194	34	0 05	0 07	— 1 D +	
			O S	? 5/ 8	0247	37	0 07		— 1 5 D +	
8	21	F	O D	2 5/ 7 5	0167	29	0 06	0 14	— 20 D	
9	27	M	O S	3 5/ 8	0?44	21	0 05		— 3 5 D	
10	13	M	O S	2 5/ 8 5	0183	41	0 12	0 14	— 1 25 D +	
11	59	M	O D	5 0/10	0182	19	0 10	0 11	Em	
			O S	5 0/10	0182	19	0 11	0 14	— 1 5 D	L G 2
12	46	M	O D	5 0/11 5	0080	25	0 06	0 11	— 10 D	Normal
			O S	6 0/11 5	0139	19	0 16	0 ?4	— 12 D	
13	37	M	O D	4 0/ 9	0177	22	0 11		— 20 D	Normal
			O S	4 0/ 9	0172	??	0 27		Em	
14	51	M	O D	3 0/ 8	0173	26	0 10		— 3 D	
			O S	2 5/ 7 25	0203	27 5	0 08		— 1 5 D	
15	?3	F	O D	2 5 7	0238	26	0 10		— 1 25 D	
			O S	0/ 6 5	0231	?8	0 13		— 0 75 D	
16	20	M	O D	2 5/ 9 5	010	1?	0 04	0 07	— 3 5 D* +	
			O S	4 5/11	0155	32	0 07	0 10	— 2 5 D +	

Correction for C — value was made only *in* eyes which were more su picious + Tonometer reading with 7 5 and 15 Gm weights

* *Post iride* tomy and cautery OU but *myopic* was present prior to operation

L G 1 = Glaucoma existed for three years before the ophthalmologist realized it Marked cupping and atrophy of the optic disc associated with marked visual and field loss were observed at the time when glaucoma was recognized

L G 2 = Early cupping of the optic disc O D and normal O S Further investigation revealed other evidence of glaucoma (impaired *outflow* f c lity and elevated ocular tension applanat on tonometer tension as ?5 5 mm Hg O D and 16 *mm* Hg O S upper arcuate *scotoma* and pos tive water dr nking test) *He* was declared normal rather than myop c twice during the past seven months by an ophthalmologist

INCIDENCE OF GLAUCOMA

It is interesting to note that two early cases and one suspected case of open angle glaucoma were observed in the myopia group, three established and two suspected early open angle glaucomas were found in the normal eye group incidentally All of these eight cases were not included in the 570 eyes mentioned above Incidence of glaucoma was 1 08% and 1 24% respectively

Myopia with glaucoma Among four early open angle glaucoma (including one suspected) cases in the myopia group, two were excessive, and two were mild myopes

II GLAUCOMATOUS EYE

A group of 16 myopic patients (29 eyes) associated with primary open angle glaucoma were investigated and the findings are shown in Table III on page 1297

COMMENT

Coefficient of scleral rigidity (*E*) varies not only in a variety of ocular diseases but also in subjects with normal eyes Therefore to determine the scleral rigidity is essential in the evaluation of intra ocular pressure The average coefficient of scleral rigidity in normal eyes has been reported as 0 0215 (Friedenwald and Kronfeld), 0 0217 (Drance) and 0 0204 (Kishimoto et al) The difference between 0 0215 and 0 0204 is statistically not significant (Kishimoto et al) [7] The average coefficient of scleral rigidity in normal eyes among Chinese was 0 0205 and is in agreement with Kishimoto et al and Friedenwald Therefore, the 1955 Calibration (AAOO) would be equally acceptable to a Chinese population

Friedenwald has investigated the coefficient of scleral rigidity in normal eyes in four age groups 15–30, 31–50, over 50 and over 60 years respectively The greater value of *E* was observed in the older group He also stated it is evident that an increasing rigidity of the ocular coats was characteristic of advancing age This change is first perceptible in the fifth decade, and it is certainly not uniform for all individuals, since even among persons of over 80 years a considerable number are found whose ocular rigidity is not greater than that of the average young normal adult [11] Drance investigated ocular rigidity in 1,011 normal eyes with applanation tonometer and stated that $E = 0\ 0217$ and found no relationship to age [10] Kishimoto et al [7] stated that scleral rigidity showed no relation to age in 216 normal eyes Schneider et al [9] reported that there does not appear to be an appreciable increase in *E* in aged patients Unfortunately they have investigated only suspected glaucoma patients, not normal eyes Therefore their data could not be considered of much use in evaluation of coefficient of scleral rigidity in normal eyes

The coefficient of scleral rigidity of the normal eyes in the present series showed a highly significant tendency to increase with age The frequency of age distribution of varying degrees of rigidity and the

cases showed lower scleral rigidity However, the outflow facility in those three patients (5 eyes) was remaining impaired after scleral rigidity correction (cases I 12 and 16 Table III) It is obvious that the data of excessively myopic eyes with glaucoma investigated in this series would have been more agreeable had this segment case been available for investigation

Grant [15] has advocated that the use of the *Po*/*C* ratio for differentiating glaucomatous and non glaucomatous eyes, with the dividing line about 100 when using the 1955 calibration Using the uncorrected value for *Po* and the uncorrected value for *C* the ratio comes out about the same as when both values are corrected for abnormalities of scleral rigidity According to his suggestion I have plotted the excessively myopic, both glaucomatous and non glaucomatous eyes with lower scleral rigidity (Table 2 and 3) and all of the myopic eyes with glaucoma (Table 3) into the diagrams below which are in agreement with and further supported Grant s work (Graphs I and 2)

The advantages of the *Po*/*C* ratio for differentiating glaucomatous and non glaucomatous eyes are simple convenient and helpful in management of myopic patient at daily office practice

It is often emphasized that the myopic eye represents a special problem in the management of glaucoma Many myopic eyes have gone blind from primary or secondary glaucoma without the patient or ophthalmologist being aware of the existence of glaucoma

This statement was apparently true in cases 1 and 12 of the table III The reason for this difficulty are (1) the distance between level of lamina cribrosa and retina in myopic eyes is much less than in normal or hyperopic eyes (2) *E* value is usually somewhat lower in myopic eyes than in normal eyes and (3) visual field abnormalities are induced by the large conus and choroidal atrophy in myopes Furthermore to interpret the appearance of the disc in high myopia is more difficult than in normal eyes if myopic cupping and large conus are present Many of these discs look atrophic and the myopic conus may add to the confusion However, I would agree with Goldmann s opinion that glaucomatous cupping in myopic eyes usually begins or is detectable at the nasal side of the optic disc and may be associated with displacement of vessels [13] Chandler has often said that the way to detect early cupping is to take a good look with the ophthalmoscope not just a brief or quick examination [14] Therefore careful fundoscopic investigation of the optic disc and the *E* influence on ocular tension and *C* value if kept in mind should be adequate in handling myopic patients with or without glaucoma It may be emphasized that (1) in management of excessive myopia the possibility of early glaucoma should be kept in mind especially in elder individuals and (2) in evaluation of ocular tension in myopia the scleral rigidity influence should be considered especially in case of myopic cupping However the glaucoma incidence is not greater in excessive myopia than in normal eyes

rigidity distribution curve for different age groups in normal eyes are shown in Figure 1 — *A* and *B*. This finding is in agreement with Friedenwald's work but not with the other.[7 10]

It has been reported that scleral rigidity in high myopic (more than — 10 D) is lower than that of normal eyes.[1 6 9 11 14] 274 myopic eyes were investigated in this series and the findings are in agreement.[1 6 9 11 14] The higher the degree of myopia, the lower the *E* value was observed (statistically, the difference of mean of *E* value is highly significant) (Fig 2 — *A* and *B*). Diaz Domingue[5] investigated the relationship of glaucoma and high myopia. He performed tonography in 25 of 100 patients with high myopia and ocular tension below 21 mm Hg. Of the 25 patients only eleven had normal outflow facility. According the Bock and Stepanek[8] in 57 excessive myopic eyes with suspected glaucoma, diagnosis was established in 35 with the help of tonography. This fact would make one wonder whether the glaucoma incidence really is that high (more than 50%) in high myopia. If so, a large per cent of high myopic eyes would have lost their sight or become blinded over a period of years. However, clinically we have not observed this condition nor the incidence of glaucoma is any higher than that of normal eyes. Two of eleven tonographed excessively myopic eyes (Over 10 D) showed decrease in outflow facility in this series and were found to be well within normal range after scleral rigidity correction and showed no other evidence of glaucoma during the past two year follow up. Therefore, one would assume that many of the high myopes in reports mentioned above would turn out to have normal outflow facility if the scleral rigidity correction was made as Moses and Becker have suggested.[6]

For further comparison a number of unilateral myopes were investigated. Coefficients of outflow facility were found low in four of 15 excessively myopic eyes but not low in 15 mild myopes. Of four seeming to have decreased outflow facility three were actually normal after scleral rigidity correction and one showed borderline diurnal variation of ocular tension and drinking test in addition to the impairment of outflow facility after the scleral rigidity correction. Therefore early open angle glaucoma was suspected (or established) in this case (Table II, case 7).

A total of 26 excessive myopes (11 bilateral 15 unilateral) have received tonography and six of these cases showed low outflow facility but five actually had a normal outflow facility after the scleral rigidity correction. In one case early open angle glaucoma was established. The cases of excessive myopia existed for years and have demonstrated no significant evidence of glaucoma. This fact well demonstrated that outflow facility with uncorrected scleral rigidity in eyes with excessive myopia would offer little of value in the early diagnosis of glaucoma and may be even dangerous if one would use this kind of outflow facility as an important diagnostic criterion or sole guide in determination of necessity for operation.

A group of 16 myopic patients (29 eyes) with primary open angle glaucoma were received routine glaucoma work up and three of these

cases showed lower scleral rigidity However the outflow facility in those three patients (5 eyes) was remaining impaired after scleral rigidity correction (cases 1, 12 and 16 Table III) It is obvious that the data of excessively myopic eyes with glaucoma investigated in this series would have been more agreeable had this segment case been available for investigation

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A group of 16 myopic patients (29 eyes) with primary open angle glaucoma were received routine glaucoma work up and three of these

SUMMARY

The Coefficient of scleral rigidity in 570 normal bilateral myopic and unilateral myopic and in 29 myopic with primary open angle glaucoma eyes was evaluated by the method of Friend nwald using only the schiotz tonometer and comparing readings with 2 weights

In normal eyes the mean value of coefficient of scleral rigidity was found to be higher in the elder age group There is no significant difference of mean value of coefficient of scleral rigidity between Chinese and Westerners A lower the coefficient of scleral rigidity was observed in excessive myopia but no significant difference was found between normal eyes and those with mild myopia It is also true in myopia eyes with primary open angle glaucoma.

It is suggested that in management of excessively myopic patients the possibility of abnormal scleral rigidity and its influence on apparent intraocular pressure and outflow facility should be kept in mind

Using the Po/C ratio with the dividing line about 100 for differentiating glaucomatous and non glaucomatous myopic eyes as advocated by Grant are convenience and helpful in daily office practice

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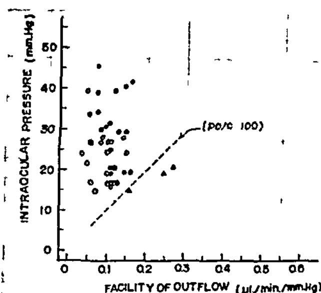
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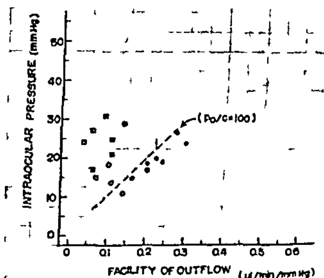
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GRAPH 1 Twenty seven glaucomatous eyes with myopia and two non glaucomatous eyes with myopia were plotted with Grant's diagram $Po/C = 100$ dividing line to differentiating glaucomatous and non glaucomatous eyes

Open circle = uncorrected *Po* and *C* closed circle = corrected *Po* and *C* in glaucomatous eyes Open triangle = uncorrected *Po* and *C* closed — triangle = corrected *Po* and *C* in non glaucomatous eyes



GRAPH 2 Three glaucomatous eyes with excessive myopia and five non glaucomatous eyes with excessive myopia were plotted as in graph I

Open squal = uncorrected *Po* and *C* closed squal corrected *Po* and *C* in glaucomatous eyes Open circle – uncorrected *Po* and *C* closed circle = corrected *Po* and *C* in non glaucomatous eyes

It is interesting to note that this new technique was evolved as a result of the author s observing four cyclodiathermy dialysis patients develop an acute attack of glaucoma from pupillary block

TECHNIQUE

A drop of pontocaine 0 5% is instilled into the conjunctival sac every four minutes for four times Following the usual face preparation anesthesia is obtained by Van Lint's method, together with retrobulbar injection of 2 cc of 2% xylocaine through the skin at the inferotemporal margin of the orbit

A lid speculum is put into place, and the superior rectus suture is inserted The conjunctiva and Tenon s capsule are incised 5 mm from the limbus the incision extending either from 11 o clock to 3 o clock position or from 1 o clock position to 9 o clock Both layers are carefully separated from the sclera with Steven's scissors extending forward to the limbus The posterior lip of the conjunctival incision is dissected from the sclera to as far back as 2 to 3 mm avoiding the area of the superior rectus muscle The flap of Tennon s capsule and conjunctiva is then reflected using a 6–0 black silk suture All persistent bleeders are mildly cauterized to prevent blood from trickling into the anterior chamber later

With a Bard Parker No 15 blade a scratch incision about 4 mm in length and 0 5 mm in depth is made perpendicular to the surface of the sclera and 6 mm from the limbus Then two rows of partial penetrating diathermy applications two on each side arranged in a V shaped fashion are made, ultilizing a 1 mm pin elect rode and 35 milliamperes of current (Walker Unit) Currently, the author uses a four pinned electrode prepared by Storz Co The length of application of electrode should not exceed 3 to 4 seconds

Then a single armed 6–0 black silk suture is inserted 4 mm behind the posterior lip of the conjunctival incision through the posterior lip of the scleral scratch incision then looped and through the anterior lip of the scleral incision Finally this suture is continued through the posterior lip of the conjunctival incision 1 mm in front of the insertion of the other end of the suture At this stage of the surgery the scratch incision is made deeper until its midsection reaches the darkish outer border of the ciliary body A trial insertion of the cyclodialysis spatula is then made to verify whether or not the line of cleavage between the sclera and ciliary body has already been established (no actual cyclodialysis yet)

Then at the 12 o clock position an ab externo scratch incision is made perpendicular to the scleral surface 1 mm behind the limbus After a 6–0 black silk suture has been preplaced as in the aforementioned scleral scratch incision the ab externo incision is deepened until the chamber has been entered This stage is usually ushered in by a tiny iris prolapse If no iris tissue presents gentle pres sure should be applied 1 mm above the ab externo incision

CYCLODIATHERMY-DIALYSIS IRIDECTOMY

A Preliminary Report of One-Hundred nine Eyes Undergoing This Operation

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This paper presents a combination method for performing a filtration operation for angle closure glaucoma that has lasted more than 36 hours as well as for chronic simple glaucoma, especially when the angle tends to be narrow. It is a modification of cyclodiathermy dialysis, a method advocated by the author [1] for glaucoma patients, particularly those with contracted visual fields and definitely diminished outflow facility. A "tunnel" is produced connecting the anterior chamber and the suprachoroidal space by multiplethrust cyclodialysis and by cyclodiathermy applications along the border of the proposed "tunnel". In addition to this, a peripheral iridectomy is performed through an ab externo incision at 12 o'clock position before the cyclodiathermy dialysis is completed on the upper outer or upper inner quadrant.

The combination of iridectomy and cyclodialysis is not altogether new, having been suggested by Czermak [2] in 1906. Other advocates of this, although in various modifications, were Hauber [3], Queiroga [4], Wootton [5], Wheeler [6], Goldmann [7], Allen [8], and Posner [9].

Although the rationale for combining iridectomy and cyclodialysis has not been completely clear, the following points have been considered: (1) When combined with cyclodialysis, the peripheral iridectomy tends to deepen the anterior chamber, thereby enhancing permanence of the internal fistula. (2) Since a shunt is made between the anterior and posterior chambers, pupillary block is prevented. (3) There may be improvement of filtration through the trabecular spaces that may occasionally be torn open by the cyclodialysis and possibly by the iridectomy if basal enough.

In the new operation herein described the author adds cyclodiathermy to the already well known cyclodialysis iridectomy combination, which is done through separate incisions. The rationale for the diathermy along the proposed "tunnel" is to promote "pillar formation" that will not only prevent hypotony but also lessen the chances for complete reattachment of the ciliary body to the sclera. Moreover, the diathermy application diminishes the danger of surgical hyphema. The subsequent ciliary body atrophy is not of much significance, as the area covered by the diathermy is approximately 1/16th of the entire ciliary body area.

The following criteria were used in evaluating results obtained from this procedure (1) Tension was normalized — not higher than 25 and not lower than 7 mm Hg Schiotz (2) Vision was preserved or improved (3) Visual fields were maintained or improved (4) Aqueous outflow facility was increased (5) A cleft or tunnel entrance however small was demonstrable by gonioscopy (6) The patient himself was satisfied over the result — headaches gone, eye not disfigured, no need for diamox and the like

The results in controlling tension have been quite gratifying Except in five patients the pressure was normal two months or longer after operation The average intraocular pressure reading was 42 mm Hg Schiotz before surgery, this dropped to 15 (average) after surgery The incidence of hypotony was only 2, but this was only temporary

Vision was preserved in all patients although in the first two weeks following surgery a few had blurry vision resulting from transient astigmatism It is noteworthy that the three patients with just light perception before surgery did not lose this ability, but rather picked up in light perception field, the vision improving to CF in one In the two hypotony cases vision improved to 20/? as the pressure came back to normal

In the great majority of the cases, the visual fields expanded concentrically or segmentally by 5 to as much as 15 degrees, and in patients with only glaucoma the blindspots stopped enlarging or became almost normal in size again This was observed especially in those patients in which the pressure was brought down to 8–12 mm Hg Schiotz This finding is in accord with that of L..goss)'s [30] However after the lapse of 2 to 3 years following surgery, a few showed some visual field loss

Excepting six all eyes undergoing tonography both preoperatively and postoperatively showed some improvement in the facility of outflow Gonioscopy revealed the presence of a cleft of varying sizes in all these eyes It should be concluded however that facility of outflow is directly related not to the apparent size of the cleft but rather to the actual area of drainage which is extremely difficult to evaluate even gonioscopically or biomicroscopically

Patients that found no relief from medications (drops ointment pills) were very grateful for the feeling of well being obtained after the surgery and for the diminution or even discontinuance of medications Three patients diagnosed by general practitioners to be suffering from labyrinthitis proved the most grateful of all the patients undergoing this procedure

COMPLICATIONS

Complications were never serious except in one case of rubeosis iridis in which glaucoma recurred two weeks after surgery due to persistent and repeated postoperative hyphema Primary hyphema

The iris root is carefully grasped for peripheral iridectomy avoiding too much loss of aqueous The iris is gently reposited in a milking fashion, until the pupil becomes roundish again The limbal preplaced suture is now tied over the conjunctival flap If considerable aqueous has been lost, normal saline or air should be injected to reform the chamber This will prevent lens injury and undue hyphema when cyclodialysis is subsequently done

Then cyclodialysis is carried out by inserting the cyclodialysis spatula gently and by following the line of cleavage until the scleral spur is passed and the spatula tip is barely seen in the periphery of the anterior chamber Steady fixation of the anterior lip *of the scleral incision should* be done while the spatula *is* being pushed along and is hugging the inner scleral surface Without withdrawing the spatula completely, seven to nine thrusts are made in an overlapping fashion, usually aiming at the 12 o'clock position and then working towards the 3 or 9 o'clock positions, depending on which quadrant and which eye is being operated on It is important to avoid making thrusts directly in front of the tendon insertions in order to spare the ciliary vessels from damage If the thrusts have been done correctly, there is no need for sweeping the spatula side *to side,* as *they may rip some branch vessels open*

The scleral incision is then closed by cautiously pulling the ends of the preplaced suture and tying a square knot snugly The incision in the conjunctiva and Tenon s capsule is closed by *continuous 6–0 black silk suture Neosporin* and *pilocarpine ointments* are instilled Both eyes are patched to promote ocular rest and thus prevent postoperative hyphema

PRESENTATION OF DATA

The operation was performed upon 109 eyes of 79 patients, 35 of whom were females Racial distribution was as follows Caucasian — 35, Negro — 16, Mexican — 9, Filipino — 18, Japanese — 1 As to type of glaucoma, there were 103 eyes falling under the category of PRIMARY, and only 6 eyes under SECONDARY *Of the* PRIMARY, 83 were chronic simple, 15 angle closure, and 5 absolute *Of the* SECONDARY, 2 eyes had developed acute glaucoma from eye injury, 1 from rubeosis iridis 1 following cataract extraction in which no iridectomy was performed and 2 from unknown causes

As much as possible, glaucoma work up was done in all the patients before and after glaucoma surgery This consisted of (1) thorough history and careful physical examination (2) visual acuity tests, (3) fundoscopy, with emphasis on cupping of the nerve head and the status of the retinal vessels, (4) repeated tonometry, (5) visual field investigation with small and large targets (6) slit lamp examination to determine depth of chamber and *status* of the lens (7) gonioscopy, and (8) tonography Provocative tests were resorted to only in borderline cases

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(very slight) occurred during operation in about one fourth of the 109 eyes undergoing surgery, while secondary hyphema was seen on the second or third postoperative day in 5 eyes In all the eyes with slight hyphema during surgery, the anterior chamber cleared completely, or almost so, on the first postoperative day

Another complication that required close attention was uveal reaction during the first few days after surgery This required topical and/or systemic steroids In two eyes with moderate uveal reaction leading to transient posterior synechiae, spotty cortical lens opacities were also observed No malignant glaucoma, no sympathetic ophthalmitis, and no eye infection occurred [1]

INDICATIONS AND CONTRAINDICATIONS

Cyclodiathermy dialysis iridectomy surgery is ideal for patients with an acute attack of glaucoma (angle closure) that has persisted over 36 hours It is ideal for chronic simple glaucoma with rather narrow angle, or where there is a threat of peripheral anterior synechia formation Secondary glaucoma resulting from blockage in the angle by synechiae or inflammatory deposits may be controlled by this type of surgery In absolute glaucoma, in which the presence of an intraocular tumor has been ruled out, this procedure might save the eye from enucleation

On the other hand, this procedure is contraindicated in rubeosis iridis regardless of etiology, and in eyes with cataracts It is extremely dangerous to perform the peripheral iridectomy portion of this procedure in cases of aphakia in which no iridectomy had been previously done

MERITS OF THE OPERATION

The operation is simple and safe, and can be finished in 15 to 20 minutes Since the pupillary sphincter is preserved and since no iris pillar is incarcerated the cosmetic appearance is quite satisfactory and annoying glare and foreign body sensation from big blebs are avoided The incidence of hypotony, malignant glaucoma sympathetic ophthalmitis, and eye infection is definitely less than in other glaucoma operations This procedure may be done either in the nasal or temporal quadrant

SUMMARY

A modified glaucoma operation consisting of cyclodiathermy cyclodialysis and peripheral iridectomy is described Indications contraindications complications and merits of the operation are enumerated and discussed Thus far the procedure has been quite effective in controlling ocular tension in 78 of 79 glaucoma patients The operation however cannot be evaluated fully until more time has elapsed and other surgeons have had an opportunity to report their own results

We found out that the basic condition securing the successful result of the operation is the close fitting of the transplanted mucosa flaps to the sclera We achieved this fixing the mucosa flaps to the sclera by means of episcleral sutures instead of sewing them to the con junctiva or rectus muscles as it had been performed formerly Such fixing provides good healing of the transplanted flaps to the sclera

In many cases it is sufficient to perform only the first operation of removing symblepharons to eliminate both partial and extensive adhesions of one and sometimes even of two eyelids

This operation results in the restoration of the fornices the correct position of the eyelids and a good closing of the rima palpebrae

If the operation has been performed owing to total symblepharon of both the eyelids then soon after the operation there takes place a scar shrinking of the mucosa transplanted on the wound surface of the eyelids and as a result an entropion and lagophthalmos reaching sometimes 10–12 mm develops

The inability to close eyelids brings on the drying out of the operated eye the patient feels the deterioration in the state of his eye after the operation

We worked out the second operation — the econd stage of removing the symblepharon performed three weeks later after the first one this operation permits to remove completely this grave state It consists in separation of the scar shortened mucosa its elongation by means of a piece of the buccal mucosa which is common for both lids and blepharorraphy no shrinking of the transplanted flap takes place as there is one piece of the mucosa and blepharorraphy Three four months later when the process of scarring are already over the lids are incised along the line of their suturing

The stages of surgical treatment described here vary depending upon the gravity of the injury and permit us to operate successfully even the gravest forms of symblepharons which up to now were considered incurable

In this report we dwell upon the results of treating 500 patients who had 555 eyes operated 222 patients (44 4%) were under our observation from 1 to 10 years 52 (10 4%) — from 6 to 12 months and 226 (45 2%) — less than 6 months Prolonged observations over more than the half of the operated patients give the possibility to draw final conclusions on the efficiency of our method of surgical treatment of extensive and total symblepharons The operated patients were mainly of younger age group 331 (66 2%) patients were at the age from 20 to 40 73 (14 6%) — from 10 to 20 years old

The character of eye injury was very serious 219 patients (43 8%) had both the eyes injured 249 patients (49 8%) had been unsuccess fully operated in other ophthalmological institutions Only on 99 eyes (17 8%) out of 555 operated ones there was a partial symblepharon of either one or two eyelids on 163 eyes (29 4%) there was either an

EFFICIENCY OF OUR METHOD OF TREATING GRAVE CONSEQUENCES OF EYE BURNS

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In the Soviet Union extensive work is carried out on safety and protection of health of people working in plants where eye burns may occur owing to special kind of work Nevertheless accidents still take place Sometimes eye burns result in deep changes, leading to deterioration of vision and even blindness The loss of vision in the majority of such cases is due to the adhesions of the lids with the eye globe and the development of leucomas Changes in the posterior section of the eye occur less frequently, mainly after chemical burns with ammonia, aniline, soda and some other chemicals

Thus, ophthalmologists have to deal mainly with symblepharons, and leucomas in patients with consequences of eye burns

In principle there is the possibility of restoring or improving the vision in such patients after removing symblepharons and leucomas

However, up till now it was a very serious problem as there was no effective method of removing extensive and total symblepharons

In books on eye surgery as well as in articles of separate authors there is no effective method of removing symblepharons of different gravity (A Elschnig, 1922, V P Odintsov and K H Orlov, 1933, H Thiel, 1945, A A Colen, 1950 Arruga, 1953, A Callahan, 1955, A F Rumiantseva, 1956, H B Stallard, 1958 etc)

We worked out the method of surgical treatment of extensive and total symblepharons which gave favourable results (N S Pouchkovskaya, 1951, 1954, 1955, 1960)

The efficiency of this method was confirmed by G V Legueza (1955–56)

At present we possess extensive clinical data in this direction Over 500 patients with grave consequences of eye burns were operated after this method in the Filatov Institute now we may draw definite conclusions on the efficiency of this method I shall dwell upon the main principles of our method which consists of one or two operations depending on the extension of symblepharon In the first operation incision of the adhesions and transplantation of mucous membrane separately on the wounded surface of the sclera and on the wounded surface of the lids is effected

Table 1 — Results of Surgical Treatment Depending on Initial State of Operated Eyes

Initial State of Operated Eyes	Number of Eyes	Results of Treatment Number of Eyes	
		Success	Failure
Partial symblepharon of one or both eyelids	99	99	—
Extensive symblepharon of one eyelid	115	111	4
Extensive symblepharon of both eyelids	145	140	5
Total symblepharon of one eyelid	48	48	—
Total symblepharon of both eyelids	109	99	10
Total symblepharon and ankyloblepharon of both eyelids	39	36	3
Total	555	533 (96%)	22 (4%)

after burns Here are some data out of the case histories of the patients operated by us

Patient P 22 years old case hist Nos 35810 38577 Burn of the left eye with soda two years ago Extensive symblepharon of both the eyelids overgrowth of scar tissue on the cornea vascularized leucoma of the left eye visual acuity equals to correct light projection (Fig 1) The right eye is healthy At first the symblepharon was removed on



Fig 1 Patient I Extensive symblepharon of both the eyelids overgrowth of scar tissue on the cornea vascularized leucoma of the left eye

extensive or total symblepharon of one eyelid, on 25 eyes (4 5 8%) there was either an extensive or total symblepharon of both the eyelids and on 39 eyes (7%) there were total symblepharons and ankyloblepharons of both eyelids

On all the eyes there were total or partial vascularized leucomas, *in many cases there was the overgrowth of scar tissue on the cornea*

Burns with lime occupied the first place — 163 patients (32 6%), then there were burns with melted metal — 96 patients (19 2%), with alkali — 84 patients (16 8%) and *other substances — 50 patients (10%)*

The gravity of the initial state is evident from the visual acuity of the operated eyes that equalled

wrong *light* projection	on 212 eyes,
correct light projection	on 181 eyes,
counting fingers close to face	on 43 eyes,
0 01 — 0 03	on 56 eyes,
0 04 — 0 06	on 16 eyes,
0 07 — 0 1	on 13 eyes,
over — 0 1	on 34 eyes

What were the results of the surgical treatment?

Successful results were obtained on 533 eyes (96%) out of 555 operated eyes We consider successful the results of the cases of surgical treatment when the fornices have been restored and the normal position of the eyelids and complete closing of the eyelids have been achieved

The *fornices* were restored on *remaining* 22 eyes *(4%) but as we* could not obtain complete closing of the eyelids we consider that the surgical treatment in these cases was not successful

Thus, the total percentage of the success amounts to 96 Now let us analyse the results of the treatment depending upon the initial state of the operated eyes presented in Table 1 (See page 1311)

As the table shows the removal of partial symblepharons occupying up to *1/3* of the eyelid *surface (99 eyes) resulted in 100%* success In cases with extensive and total symblepharons of one eyelid and extensive symblepharons of both the eyelids *(308 eyes) successful results* were obtained on 229 eyes, i e in 97 1%

In case of symblepharons and ankyloblepharons of both eyelids (148 eyes) successful results were obtained on 135 eyes, i e in 90 6%

These data show that our method of surgical treatment of symblepharons is quite effective and *in majority of cases permits to remove* even the gravest adhesions formed after eye burns

The effective method of removing adhesions permitted *us to* perform widely the operations of keratoplasty to such patients As our numerous observations showed lamellar keratoplasty proved to be the most effective method of keratoplasty in case of vascularized leucomas



Fig 5 *Patient S after the removal of symblepharon and peripheral lamellar keratoplasty on the right eye*



Fig 6 Patient S Right eye after peripheral lamellar keratoplasty

cornea, total vascularized leucomas of both the eyes Visual acuity equals to correct light projection on both the eyes (Fig 7) At first the symblepharon on the left eye was removed (Fig 8) Then total



Fig 7 Patient S Extensive symblepharon of the upper lid overgrowth of scar tissue on the cornea of the left eye



Fig 8 Patient K. After the removal of symblepharon on the left eye

lamellar keratoplasty was performed After the transplantation of the cornea the visual acuity on the left eye increased to 0 08 Observations lasted for two years (Fig 9)



Fig 9 Patient K. Left eye after total lamellar keratoplasty

the left eye (Fig 2) Then the operation of peripheral lamellar kerato plasty after our method was performed (N A Pouchkovskaya, 1955, 1960) The central part of the cornea became transparent after the operation Visual acuity equals 0 2 Observations lasted for 1½ years (Fig 3)



Fig 2 Patient P Left eye after the symblepharon has been removed



Fig 3 Patient P Left eye after peripheral lamellar keratoplasty

Patient S 25 years old, case hist Nos 9081, 11520, 13397 Burn of both the eyes with melted metal a year ago Total symblepharon of both the eyelids and ankyloblepharon of the right eye, visual acuity equals to wrong light projection Ectatic leucoma, secondary glaucoma of the left eye, visual acuity equals to light perception (Fig 4)



Fig 4 Patient S Total symble pharon and ankyloblepharon of the right eye

At first two basic operations were performed on the right eye to remove the symblepharons and then peripheral lamellar keratoplasty was performed after our method

The cornea corresponding to the pupil region became transparent due to the operation Visual acuity equals to 0 09 Observations lasted for 3 years (Figs 5, 6)

Patient K 22 years old, case hist Nos 29158, 32327 39055 36019 Three years ago — a burn of two eyes with lime Extensive symblepharon of the upper eyelid overgrowth of scar tissue on the



Fig 5 Patient S after the removal of symblepharon and peripheral lamellar keratoplasty on the right eye



Fig 6 Patient S Right eye after peripheral lamellar keratoplasty

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The above data show that our method of removing symblepharons followed by keratoplasty makes possible to obtain the restoration of vision even in some patients with very grave consequences of eye burns, i e to obtain success in the patients whom as it seemed at first it was impossible to help

Our numerous observations permit to recommend to use widely our method of removing symblepharons followed by optic lamellar keratoplasty in case of grave consequences of eye burns in the practice of ophthalmologists

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1 Pouchkovskaya, N A. Surgical treatment of extensive and total symblepharons *Vestn Oftal* v 30 no 4

2 Pouchkovskaya, N A. 1955 Transplantation of the cornea after removal of extensive and total symblepharons Scientific Papers (Utchenii Zapiski UEIGB v III)

3 Pouchkovskaya N A 1960 Transplantation of the cornea in case of complicated leucomas Kiev

TRAITEMENT DES BRULURES DES YEUX

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Directeur de la Clinique Ophthalmologique pres de l Institut de Medecine de Gorki

Il existe beaucoup de moyens medicamentaires et operatoires pour traiter les brulures graves On recommande à faire une section dans la conjonctive troublee sa separation En appliquant ces opera tions nous n avons pas obtenu ni bon ni tres mauvais resultats Certain auteurs dans le but d empecher une commissure ainsi que a l effet thérapeutique couvrent l oeil brule par protheses en materiaux divers Nous pouvons constater que lors des brulures graves aucuns prothèses n empechent les procedes de cicatrisation et le prothese est jete dehors, pousse hors de l orbite Nous avons essuye les protheses de differente forme cuvettes d Illogue, platines plastiques en verre, en caoutchouc le pellicule ovalbumine le papier etc

Nous croyons que leur application est inutile et parfois meme aggrave le procedé de brulure comme l opération Denaigue car, selon nos observations dans le cas ou la muqueuse adhere la thera peutique complexe actuelle assure les meilleurs resultats

Nous avons surveillé dans les conditions d un stationnaire 724 malades ayant les brulures des yeux En 92% c etaient les brulures du 2nd et 3me degré d ailleurs 41% de malades avaient brûlures de deux yeux Les brulures chimiques sont constatées en 78 9% de cas

En analysant les resultats nous pouvons constater que l adminis tration du sang ou serum de sang par l instillation et dans les cas plus graves par injection sous la conjonctive donne de bons resultats

Nous avons appliqué un melange compose du sang, vasodila tateur penicilline et le temps dernier — antibiotique imanine substance anésthesique bloquant vitamine En administrant un tel melange antibrulure il ne faut pas avoir une attitude banale, car la proportion des components doit etre variée selon la predominance de l un ou de l autre facteur adu cours de procede de brulure

En général la formation des foyers nécrotiques arrive tot au cours de premiers 3-5 jours Evidemment cette formation est liée avec la formation de thrombus dans les vaisseaux sanguins C est pourquoi au cours de premiers 3-4 jours à coté d autres moyens medicamen taires il est utile d administrer les resorptives les préparats empechant l accélération de vitesse de la coagulation du sang du type d anti coagulants

The above data show that our method of removing symblepharons followed by keratoplasty makes possible to obtain the restoration of vision even in some patients with very grave consequences of eye burns, i e to obtain success in the patients whom as it seemed at first it was impossible to help

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A NEW OPERATION FOR FRACTURE OF THE OPTIC CANAL AND DISEASES OF THE ORBITAL APEX

TIKASI SATO, M D
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According to statistics published by the World Health Organization in 1962 the number of deaths by accidents has been increasing every year with the traffic accidents ranking first It is said that more than 100,000 people die from traffic accidents every year

In many traffic accidents head injuries especially, fractures of the base of skull present problems In the field of ophthalmology the problems lie largely in the fracture of the optic canal Statistics compiled by the Department of Ophthalmology of Osaka University (8) showed that the number of injuries to the optic nerve ranked top of all the other injuries sustained by traffic accidents

The treatment of the fractures of the optic canal has not produced good results in the past The major principle of treatment of this type of frature has been decompression of the optic nerve The conservative treatment may have successfully relieved hematoma or the cerebral concussion due to the fracture, but has often failed to improve vision, and sometimes led to blindness

Craniotomy one of the approaches used today, leaves a scar on the forehead and not infrequently causes headaches and may even result in fatality because the dura is incised and the chiasma is reached by elevation of the brain This procedure however, merely permits the removal of the hematoma but it is difficult to remove the frag ments It permits at best, the removal of fragments only of the upper wall of the optic canal

The intranasal operation is another approach to the problem The optic canal can be reached through the nostril or the maxillary sinus This operation however allows only a limited operative field and therefore the removal of fragments is difficult The mucous mem brane may remain uncleaned and often results in infection later It is difficult to remove fragments *completely* by either method Even though it is possible, only one quarter that is 90 degrees of the circum ference of the optic canal can be explored and, there is always the risk of injuring the dura or causing infection.

I came to think of a new operative approach That is to reach the optic canal by opening the frontal sinus the ethmoid sinus and the

Un des problemes dans le therapeutique complexe des brûlures c'est une plus rapide et complete elimination du tissu nécrotisé, ce dernier diminue la gravite des iridocyclites et uveides arrivant souvent Pour eliminer les tissus necrotiques, autre les methodes mecaniques, dans les cas ou la cornée n'est pas derangee, nous avons commence d'administrer le tripsine Nous l'avons administré sous forme d'une solution 1%, dont le dissolvant etait un tampon en phosphate avec Ph = 8,04

Apres avoir nettoye les sections brûlees des tissus necrotises afin de stimuler les procedes de regeneration, il est utile d'ajuster aux preparats les nucleotides produits de fission d'acides nucleines, qui sont un des facteurs necessaires pour le developpement des cellules

Touchant de la question d'application locale des corticosteroides, nous pouvons constater, que ces preparats ne sont pas utiles sur toutes les etapes du traitement des brulures Dans les cas ou la defense inflammatoire est faible, les tissus anemiques, quand cette anémie est si grave, qu'il faut administrer les vasodilatateurs, — ces préparats sont nocifs

En periode ou il y a une reaction inflammatoire abondante, une vascularisation abondante, — leur administration est efficace

Annees dernieres, sont publies les travaux constatant que dans la cuir brulee et le serum de sang naissent des autoanticorpuscules specifiques Il y a des preuves de la presence dans le serum du reconvalescent, ayant endure la brulure, des anticorpuscules reliant le complement en regard de l'anticorpuscule de brûlure Alors, le serum de reconvalescent ayant endure une brulure, lors de son injection a un homme brule frais ou a un animal, doit exercer une action anti toxique

Les travaux experimentaux de l'institute des maladies ophthalmologiques a Odessa constatent, que le serum de sang des convalescents, ainsi que le serum de sang des lapins, immunes d une méthode certaine, — exercent une action thérapeutique lors de son injection au lapins, qui ont des brulures des yeux

Compte tenu de l'experience positive en regard de la therapeutique patogenetique plus rationnelle de la brûlure, nous avons, le temps dernier, administre avec succes les transfusions du serum ou du sang des donneurs qui ont enduré une brulure L'autosang entrant dans le melange lors de l'injection sous la conjonctive, nous avons remplace par du sang ou du serum de sang du reconvalescent ayant endure une brulure, aux intervalles entre les injections nous avons instille le serum de sang de memes donneurs

On sait, que lors des brulures des yeux les changements arrivent non seulement dans l'organe de vision, mais ils sont refletes sur l état general, la régulation nerveuse et endocrine se trouble, ce dernier doit etre retenu lors de la selection de methodes du traitement des brulures Voila pourquoi lors du traitement in loco il faut simultanement d'administrer le therapeutique generale

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I came to think of a new operative approach That is to reach the optic canal by opening the frontal sinus the ethmoid sinus and the

sphenoid sinus along the upper medial corner of the orbit This permits of a safe and satisfactory method for removal of fragments It affords a wider operative field and eliminates the necessity of opening the dura

As it required entry into the sinuses, I requested Dr Shoji Niho, rhinologist, to examine the new method and to conduct the first operation

The operation was more successful than originally expected It was learned that this operation can be applied not only to the fractured optic canal but also to rhinogenous neuritis, traumatic or rhinogenous paralysis and orbital tumor, as it cuts open the orbital apex

METHOD OF OPERATION

The key points of the operation are described below The operation of the maxillary sinus is not always necessary but may be advisable to prevent inflammation and to make further operation easy because the operation of the maxillary sinus often leads to a discovery of fragments which cannot otherwise be discovered clinically or rontgenologically (Even in the case of rhinogenous neuritis or rhinogenous paralysis, operation of the maxillary sinus as a first step may be advisable, as such diseases are often caused odontogenously In odontogenous cases, the mucous membrane is not usually affected, but osteomyelitis may develop and may require an operation of the maxillary sinus) This operation may be done by the conventional method

Following the opening of the maxillary sinus, it is advisable to open intranasally the ethmoid sinus and the sphenoid sinus as wide as possible It will make the extranasal operation to be performed later easy Care must be taken not to traumatize the lamina cribrosa Otherwise, meningitis may follow

The intranasal operation is followed by an extranasal operation Our new method begins here As first step the skin is cut from the nasal root into the eyebrow (Fig 1–A) The operation proceeds to remove the mucosal lining of the frontal, ethmoid and sphenoid sinuses, and to remove the upper inner bony wall of the orbit as far back as the optic canal (Fig 1–B, C)

During the operation, the patient may experience a sudden increase or decrease of vision Thus, a local anesthesia is necessary, for the subjective response of restoration or diminution of vision during the operative procedure is of extreme importance Operation under local anesthesia is possible in children Care must be exercised not to traumatize the trochlea and the lacrymal sac when the lining of the frontal sinus is removed The further posterior operation discloses the sphenoid sinus Its location can be determined by X ray examination

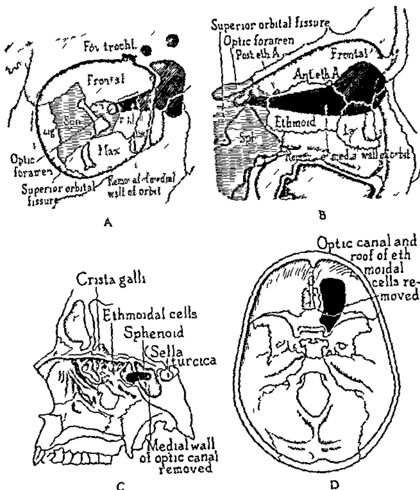


FIG 1 (A) Removal of shaded portion to enter the ethmoidal cells and the frontal sinus (B) Removal of the medial wall of the orbit to the distal end of the bony optic canal (C) Removal of the medial wall of the optic canal Shaded portion Grade I operation (D) Craniotomy Removal of the roof of the ethmoid cells and of the optic canal Shaded portion Grade II operation

The anterior and posterior ethmoid arteries now become obstacles in reaching the posterior ethmoid sinus and it must be cut with great care for hemostasis before proceeding further The optic canal will then be observed extending from the anterior lateral to the posterior medial on the upper wall of the sphenoid sinus or the ethmoid sinus The anatomy of the optic canal varies Fragments are removed in the case of fracture If the fragments are not visible, the lower and the medial wall of the optic canal are removed

When the injury is still fresh the removal of fragments or the bony wall often results in the sudden increase of vision Utmost care must be exercised not to traumatize the optic nerve

This procedure allows of removal of half of the circumference of the optic canal and often suddenly increases vision, at which time the operation may be ended This is our Grade I operation If there is no subjective improvement in vision, we now begin to unroof the optic canal This is our Grade II operation (Fig 1–D)

A craniotomy is performed opening the upper wall of the ethmoid and the sphenoid sinuses as far as the anterior clinoid process The dura is elevated, care being taken not to traumatize the lamina cribrosa, the dura, or the optic nerve Thus the upper, the lower and the medial wall of the optic canal can be removed When the operation is over, sufficient drainage is instituted and antibiotics are given both locally and generally Several weeks of bed rest is required

The vision and the visual field which improved during the operation may deteriorate in the following week due to the operative reaction, but will be restored in several months

Table I shows the period of observation after operation in 14 cases of fracture of the optic canal

TABLE 1 — *Cases of fractured optic canal*

Case	*Age (yr)*	*Sex*	*Days until Operation*	*Preoperative Vision*	*Postoperative Vision*	*Days After Operation*
1	19	M	37	0	s l	1 yr
2	25	M	6	0 03 0 04	0 4	1 yr
3	30	M	52	0 01	0 1	1 yr 10 mo
4	31	M	263	0 1	0 6 0 7	2 mo
5	31	M	14	0 02	0 4	1 yr 5 mo
6	6	M	6	0 02	0 1	1 yr 1 mo
7	9	F	5	0	0 04	1 yr 4 mo
8	67	M	102	0	0	1 mo
9	16	M	12	10 cm/n d	0 1	5 mo
10	24	M	53	0 1	0 7	2 mo
11	17	M	16	0 06	0 3	4 mo
12	32	M	5	5 cm/n d	0 1	53 d
13	30	M	25	20 cm 2m/n d	70 cm 1 m/n d	84 d
14	19	M	164	0 006	0 03	110 d

From these cases we can conclude that the fresher the injuries, the better the results This shows in Cases 1 and 7, where the vision of the persons without light perception was restored, although slightly

However such visual recovery — the recovery from no light perception — is unusual Therefore, in Case 7, six ophthalmologists confirmed the fact that the patient had no perception of light, but following the operation the patient demonstrated before the ophthalmologists at a Tokyo medical meeting that vision had been restored

In contrast, as shown in Case 8, where the patient was operated 102 days after the injury vision was not restored It was also discovered that patients with good preoperative vision have a better chance of visual recovery even with traumatic optic atrophy

This operation permits opening of the orbital apex and the bony optic canal and therefore can be applied to some other conditions We happened to experience an unexpected improvement of paralysis of the extrinsic muscle when fragments were removed This may be due to the decompression of muscles and nerves For this reason, we applied this operation to the treatment of rhinogenous neuritis (3 5, 9) and paralysis (1, 2 3 5 7 9) which were caused by the inflammation or compression of the orbital apex

Table II shows nine cases of rhinogenous neuritis Many serious cases are caused odontogenously and are apt to develop osteomyelitis and meningitis and therefore necessitate the extraction of teeth in some cases

For example in Case 7 the patients s life was saved but vision became worse In cases 7 8 and 9, the conventional intranasal operation was performed but having produced no satisfactory result, we resorted to our extranasal operation This produced a good result. In Case 9 the patient with no perception of light for two weeks following the traditional intranasal operation had restoration of vision to 0 7 after our operation Such recovery of vision from no perception of light seldom occurs in the conventional operation but in our operation success is not infrequent as indicated also in Cases 1 and 7 of the fracture cases For this reason we felt that our operation has fairly good results

In rhinogenous neuritis pus is not always evenly distributed in the sinuses One sinus may be more seriously infected than others but infection must be *completely eliminated from all* the sinuses to prevent recurrence

A histological examination of the bony wall of the optic canal removed at the time of rhinogenous neuritis revealed that noticeable inflammation penetrated from the mucous membrane through the bone of the optic canal almost to the optic nerve

The operation for paralysis of ocular muscles can also be performed in a similar manner to decompress the muscles and nerves That is to say, the sinuses must be cleaned in the case of rhinogenous

This procedure allows of removal of half of the circumference of the optic canal and often suddenly increases vision, at which time the operation may be ended This is our Grade I operation If there is no subjective improvement in vision, we now begin to unroof the optic canal This is our Grade II operation (Fig 1–D)

A craniotomy is performed opening the upper wall of the ethmoid and the sphenoid sinuses as far as the anterior clinoid process The dura is elevated, care being taken not to traumatize the lamina cribrosa, the dura, or the optic nerve Thus the upper, the lower and the medial wall of the optic canal can be removed When the operation is over, sufficient drainage is instituted and antibiotics are given both locally and generally Several weeks of bed rest is required

The vision and the visual field which improved during the operation may deteriorate in the following week due to the operative reaction, but will be restored in several months

Table I shows the period of observation after operation in 14 cases of fracture of the optic canal

TABLE I — *Cases of fractured optic canal*

Case	*Age (yr)*	*Sex*	*Days until Operation*	*Preoperative Vision*	*Postoperative Vision*	*Days After Operation*
1	19	M	37	0	s l	1 yr
2	25	M	6	0 03 0 04	0 4	1 yr
3	30	M	52	0 01	0 1	1 yr 10 mo
4	31	M	263	0 1	0 6 0 7	2 mo
5	31	M	14	0 02	0 4	1 yr 5 mo
6	6	M	6	0 02	0 1	1 yr 1 mo
7	9	F	5	0	0 04	1 yr 4 mo
8	67	M	102	0	0	1 mo
9	16	M	12	10 cm/n d	0 1	5 mo
10	24	M	53	0 1	0 7	2 mo
11	17	M	16	0 06	0 3	4 mo
12	32	M	5	5 cm/n d	0 1	53 d
13	30	M	25	20 cm 2m/n d	70 cm 1 m/n d	81 d
14	19	M	164	0 006	0 03	140 d

From these cases we can conclude that the fresher the injuries the better the results This shows in Cases 1 and 7, where the vision of the persons without light perception was restored although slightly

However such visual recovery — the recovery from no light perception — is unusual Therefore, in Case 7, six ophthalmologists confirmed the fact that the patient had no perception of light, but following the operation the patient demonstrated before the ophthal mologists at a Tokyo medical meeting that vision had been restored

In contrast as shown in Case 8, where the patient was operated 102 days after the injury vision was not restored It was also discovered that patients with good preoperative vision have a better chance of visual recovery even with traumatic optic atrophy

This operation permits opening of the orbital apex and the bony optic canal and therefore can be applied to some other con ditions We happened to experience an unexpected improvement of paralysis of the extrinsic muscle when fragments were removed This may be due to the decompression of muscles and nerves For this reason we applied this operation to the treatment of rhinogenous neuritis (3 5 9) and paralysis (1 2 3 5 7 9) which were caused by the inflammation or compression of the orbital apex.

Table II shows nine cases of rhinogenous neuritis Many serious cases are caused odontogenously and are apt to develop osteomyelitis and meningitis and therefore necessitate the extraction of teeth in some cases

For example, in Case 7 the patients s life was saved but vision became worse In cases 7 8 and 9 the conventional intranasal opera tion was performed but having produced no satisfactory result we resorted to our extranasal operation This produced a good result In Case 9 the patient with no perception of light for two weeks following the traditional intranasal operation had restoration of vision to 0 7 after our operation Such recovery of vision from no perception of light seldom occurs in the conventional operation, but in our opera tion success is not infrequent as indicated also in Cases 1 and 7 of the fracture cases For this reason we felt that our operation has fairly good results

In rhinogenous neuritis pus is not always evenly distributed in the sinuses One sinus may be more seriously infected than others but infection must be completely eliminated from all the sinuses to prevent recurrence

A histological examination of the bony wall of the optic canal removed at the time of rhinogenous neuritis revealed that noticeable inflammation penetrated from the mucous membrane through the bone of the optic canal almost to the optic nerve

The operation for paralysis of ocular muscles can also be per formed in a similar manner to decompress the muscles and nerves That is to say the sinuses must be cleaned in the case of rhinogenous

TABLE II — *Cases of rhinogenous neuritis*

Case	*Age (yr)*	*Sex*	*Preoperative Vision*	*Postoperative Vision*	*Other Symptom*	*Its result*
1	54	F	r 0 02 l 0 03	r 0 5 l 0 3	r Ophthalmo plegia externa & Exophthal mus	cured
2	34	F	r 0 02 l 1 2	r 0 6 l 1 2	r Ophthalmo plegia externa	improved
3	18	F	r 1 2 l 0 6	r 1 2 l 1 2	l Ophthalmo plegia ext & Papilla edema	cured
4	30	M	r s l l 0 006	r s l l s l	Odontogenous Headache	improved
5	7	F	r 1 0 l 0 03	r 1 2 l 1 2	Odontogenous l Papilla edema	cured
6	41	M	r 0 2 l 1 0	r 0 3-0 4 l 1 0	r Papilla edema	cured
7	40	F	r 0 7 l m m	r 0 9 l zero	Odontogenous l Ophthalmo plegia ext & Exophthalmus Meningitis	cured
8	19	M	r 1 2 l 10 cm/n d	r 1 2 l 0 1	l Papilla edema	cured
9	19	F	r 1 0 l 0 03	r 1 2 l 1 2	Odontogenous l Papilla edema	cured

paralysis In the case of fracture, the medial orbital wall shall be removed and the nerve of the extrinsic muscle shall be decompressed by gently striking the lower bone of the superior orbital fissure laterally with a hemostatic chisel The paralysis improves dramatically immediately following the decompression

This operation was found very effective in Case 1 of the fracture, Cases 1, 2, 3, and 7 of the rhinogenous neuritis and Case of the rhino genous ophthalmoplegia ( ) This operation affords a visual exami nation of orbital apex and thus enables more effective operative procedure in the case of tumor or inflammation

THE OPTIC NERVE MUST BE TREATED WITH EXTREME CARE

I accidentally experienced this in the operation for retinal detach ment, when I hooked and turned the optic nerve to cauterize the

macular rent Serious neuritis occurred followed by optic atrophy We also learned that the vision diminished suddenly when the optic nerve was exposed and stimulated accidentally by pressing or poking during the operation for fracture and rhinogenous neuritis We stopped traumatizing the optic nerve and vision was restored within 10 to 30 minutes

Compared with other nerves the optic nerve is far more vulnerable Optic atrophy which develops in sinus or brain surgery may have been frequently caused by rough handling of the optic nerve and not by damaging it as previously believed For this reason, local anesthesia is the one of choice in operations involving the optic nerve

Sinus diseases do not always affect all the sinuses It can occur in a small section of the ethmoid sinus Assuming that the optic nerve is very vulnerable such trifle distrubance could cause blurred vision If so the diagnosis of rhinogenous neuritis becomes extremely difficult

Very frequently, this operation may disclose the fragments which were not identifiable in the X ray examinations, or may lead to a discovery of the sinuitis which cannot be diagnosed through clinical examinations

CONCLUSION

1 This operation jointly devised with Dr Niho seems very effective and safe not only for the treatment of fractured optic canal but also for such diseases as affect the orbital apex such as rhinogenous neuritis ocular paralysis or tumor

2 The important points of the operation have been brought out

3 Diagnosis of sinus diseases is difficult

4 The optic nerve is sensitive and must be handled with care

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STRUCTURAL CHANGES OF THE OPTIC TRACT FOLLOWING UNILATERAL AND BILATERAL ENUCLEATION OF THE EYE BALL

GURGENIDZE R V

(Tbilisi)

The structural changes of nerve fibres both in unilateral and bilateral enucleation of the eye ball develop all along the optic tract from the optic nerve to the 17th field for the brain cortex Their study in a dynamic aspect permits to specify some points related to the course and location of the optic tract

The basic mass of the optic nerve the chiasm and the tract consists of afferent nerve fibres which in case of enucleation are liable to Wallerian degeneration and death In comparatively early periods following enucleation, a small number of remaining axial cylinders is to be found which is also a pointer to the presence of afferent nerve fibres in the peripheral portions of the optic tract

At first the crossed fibres of the optic nerve penetrate to an extent into the optic nerve on the opposite side and then proceed into the optic tract

In the caudal part of the optic tract the crossed and uncrossed nerve fibres primarily occur in the form of separate bundles whereas in the cranial section of the tract they are more or less evenly inter mingled At the same time in the caudal section of the optic tract the uncrossed nerve fibres occupy the central area while the crossed fibres are located in the medial and lateral sections of this part of the tract

Upon passing through the optic tract the afferent fibres of the optic nerve penetrate into the external geniculate body and into the superior colliculus

The abovementioned fibres end at the round and multipolar ganglionic cells of the primary optic centres The larger multipolar cells must represent the afferent neurons of the reflex arc of the optic tract

The terminal of the central afferent neuron of the optic analyser must be in the external and internal granular layers of the 17th field of the brain cortex

PLASTIC ARTIFICIAL CORNEA — A FOURTEEN-YEAR STUDY

Basic Principles Underlying Retention of Incompletely Covered Foreign Body in the Cornea

WILLIAM STONE, Jr, M D *

Approximately one hundred and fifty years ago, before the advent of homotransplantation, several unsuccessful attempts were made to use alloplastic materials as replacements for the cornea Little was done further until around 1950, when a few reports appeared on one or more cases of the use of plastic materials in either animal or human eyes

The work presented here began fourteen years ago [1, 3, 4] as a result of a phenomenon we observed during the second World War several pilots were seen with small fragments of methyl methacrylate embedded in their corneas, these were very well tolerated and did not extrude We felt, therefore, that it might be possible for the cornea to tolerate larger pieces of this transparent plastic equally as well We had had experience with incompletely covered, post enucleation implants and were confident at that time that such an implant could be maintained in the body without extrusion

EARLY EXPERIMENTATION

Various types of through and through discs were tried first (Fig 1) Approximately 25 shapes and sizes were fabricated, with



Fig 1 Various types of through and through plastic discs placed as full thickness implants in rabbit corneas 14 years ago All extruded within one to two weeks

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assorted appendages at the edges to anchor the implant in corneal tissue All of these extruded in a short time

Following this, in 1949 a disc (Fig 2) shaped to the contours of the rabbit cornea with holes in a peripheral skirt for tissue ingrowth was placed intralamellarly in rabbit corneas Figure 3 shows a portion of cornea from which a disc of this type was teased The projections

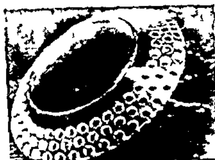


Fig 2 Disc shaped to contour of rabbit cornea with holes in peripheral skirt for tissue in growth Placed between the lamellae (1949)

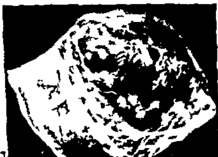


Fig 3 Rabbit cornea after an intralamellar implant (as seen in fig 2) had been teased from it Projections A and B are collagenous plugs of corneal tissue which grew through the peripheral fenestrations and held the implant firmly in place



Fig 4 Intralamellar implant in cornea of Rabbit #83 with circular opening in anterior layer of cornea down to plastic Anterior chamber can be seen clearly Photograph was taken 12 months post operative (Central opening occurred inadvertently as a result of premature rupture of sutures several days after the operation)

(A & B) are collagenous plugs of tissue which grew through the peripheral fenestrations and held the implant firmly in place ensuring its stability

EXPOSURE OF ANTERIOR SURFACE

The second phase of the work began inadvertently In one rabbit after an intralamellar disc had been placed, the sutures on one side broke loose several days post-operatively and the anterior layer of cornea receded from the central area of the disc (Fig 4) This disc

remained exposed centrally to the natural death of the animal, one year after surgery The implant did not move and the anterior chamber was at all times clearly visible through the anterior hole

We were persuaded that this exposure could be easily reproduced by deliberately opening the anterior layer, but it took two years to repeat the experiment, namely, to permanently maintain a corneal opening anterior to a plastic disc

The feature responsible for maintaining the patency of an anterior trephine hole was not immediately apparent Figure 5 illustrates the typical progression of tissue growth across the exposed surface After a hole was trephined, whether large or small, within several days a salmon colored area of tissue would appear at the edge of the trephine hole and then gradually, over a period of approximately 25-52 days, the tissue area would expand until it completely filled the opening The diameter of the trephine hole did not materially affect the speed



Fig 5 Closing of trephine hole in anterior corneal layer in front of a plastic disc (Rabbit #21 Experiment 2) A Two days post operative There is slight engorgement of vessels B Eight days post operative A distinct salmon coloring can be seen at edge of hole C Twenty one days post operative The salmon colored edge has nearly obliterated the hole D Twenty nine days post operative The hole is completely closed



with which it closed, for an 8 mm hole closed in 27 days while on an average 4 mm holes closed in 40 days The overall average closing time of these anterior trephine holes was 37 days in 44 rabbit eyes (Table I)

TABLE I — *Time of closure of trephine hole in corneal layer anterior to plastic disc as related to si e of trephine opening*

Number of Rabbits	*Size of Trephine*	*Maximum Days Open*	*Minimum Days Open*	*Average*
4	4 mm	50	30	40
19	5 mm	52	20	38
14	6 mm	50	29	38
6	7 mm	50	35	43
1	8 mm	27	27	27
			Overall Average	37

It was thought that possibly the time lapse between implantation of disc and incision of anterior hole might be the determining factor Table II shows the results when holes were placed at various intervals post implantation Trephine holes were made at periods ranging from one week to two years after the placing of the disc In 62 rabbit eyes irrespective of the extent of the interval between the two operations the holes closed in approximately 37 days

TABLE II — *Interval between implantation procedure and placing of anterior trephine hole in relation to closure of trephine hole*

Number of Rabbits	*Time After Original Operation Trephine Placed*	*Time of Closure After Trephine Placed*		
		Maximum	*Minimum*	*Average*
29	Trephined during place ment of implant	52 days	31 days	43 days
4	7 to 30 days	50 days	25 days	36 days
12	1 to 6 months	43 days	20 days	37 days
13	6 months to 1 year	48 days	28 days	37 days
4	1 to 2 years	50 days	30 days	40 days

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Fig 5 Closing of trephine hole in anterior corneal layer in front of a plastic disc (Rabbit #21 Experiment 2) A Two days post operative There is slight engorgement of vessels B Eight days post operative A distinct salmon coloring can be seen at edge of hole C Twenty one days post operative The salmon colored edge has nearly obliterated the hole D Twenty nine days post operative The hole is completely closed



TABLE III — *Diagram of various operative procedures used in cutting a hole in corneal layer anterior to Plastic Disc and results—(contd)*

Item Number	*Operative Procedure*	*Rabbit Number*	*Exp Number*	*Time of Closure after op*	*Extrusion after Placement of implant*
				Days	*Days Post op*
19	Trephined past and with evacuation first row holes	20	2	30	199
20		25	3	40	——
21		225	2	20	——
22		234	3	22	——
23	Cruciate incision with flaps sutured under	15	6	40	——
24		51	5	26	——
25		61	2	51	——
26		66	1	—	51
27	Very Superficial Incision	234	1	40	
28		58	1	—	130
29		80B	1	—	14
30		50	1	—	90
31	Thin thick Incision	61	1	47	——
32		62	1	Open 8 Mon P O	——
33		6[illegible]	1	—	72

Table III describes the types of operative procedures which were tried in an effort to produce a permanent opening in front of the implant It was not until Rabbit #62 that a hole was obtained which

TABLE III — *Diagram of various operative procedures used in cutting a hole in corneal layer anterior to Plastic Disc and results*

Item Number	*Operative Procedure*	*Rabbit Number*	*Exp Number*	*Time of Closure after op*	*Extrusion after Placement of implant*
1	Straight Cut	Experiments with this operative procedure not included Majority of experiments in Charts 1 and 2 employed this method and are noted there			
				Days	*Days Post op*
2	Angle Cut	21	1	28	—
3		25	2	42	—
4		30	1	35	—
5	Undermined with Angle Knife	29	1	40	
6		29	2	40	
7		30	2	30	—
8		42	1	35	
9	Trephined past first row of holes	15	2	48	—
10		227	1	41	
11		45	1	38	130
12		46	1	—	20
13		48	1	—	30
14		49	1	33	
15		50	1	—	90
16		51	1	45	—
17		52	1	45	114
18		54A	1	36	

Table III — *Diagram of various operative procedures used in cutting a hole in corneal layer anterior to Plastic Disc and results—(contd)*

Item Number	*Operative Procedure*	*Rabbit Number*	*Exp Number*	*Time of Closure after op*	*Extrusion after Placement of implant*
				Days	*Days Post-op*
19	Trephined past and with evacuation first row holes	20	2	30	199
20		25	3	40	—
21		225	2	20	—
22		234	3	22	—
23	Cruciate incision with flaps sutured under	15	6	40	—
24		51	5	26	—
25		61	2	51	—
26		66	1	—	51
27	Very Superficial Incision	234	1	40	
28		58	1	—	130
29		80B	1	—	14
30		50	1	—	90
31	Thin thick Incision	61	1	47	—
32		62	1	Open 8 Mon PO	—
33		65	1	—	72

remained patent for longer than 60 days (Fig 6) In this rabbit the center of the disc had been thickened (approximating an anterior projection) and it was found that the anterior trephine hole remained open indefinitely, the eye of the rabbit staying white and quiet

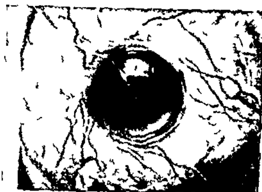


Fig 6 Rabbit #62 The first cornea in which a disc with an anterior projection was placed (Oct 1953) The thickness of the anterior projection was 1 5 mm The hole remained patent to the natural death of the animal 1 year 10 months post operative

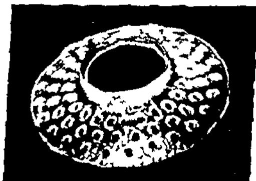


Fig 7 Implant with central anterior projection and peripheral skirt for intralamellar insertion Peripheral holes are for the ingrowth of tissue to prevent migration of the implant

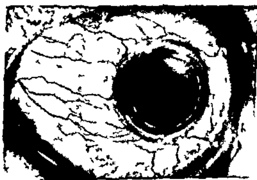


Fig 8 Implant (as seen in figure 7) which remained in rabbit cornea for 4 years 3 months to natural death of rabbit (The life span of the rabbit species limits the period of observation)

The type of disc seen in figure 7 was used at that time It has a central anterior projection, a peripheral skirt which goes between the lamellae, and peripheral holes for the ingrowth of tissue Figure 8 shows a disc of this type in a rabbit cornea for four years three months post implantation, the maximum length of time we have kept a disc in place The life span of the animal was the only deterrent to a longer implantation period

ANTERIOR PROJECTION

The experiments conducted to determine the optimum diameter of anterior nubbin and its optimal height are listed in Table IV It was found that the diameter of the projection was not influential in maintaining the implant in place and had very little to do with prevention of tissue overgrowth

TABLE IV — *Diameter and height of anterior projection in relation to patency of anterior trephine hole**

NUBBIN Width in mm		*Height in mm*	*Number of Rabbits*	*Results*
5	×	1 25	12	Open
5	×	1 00	13	Open
4 5	×	1 00	3	Open
4 5	×	7	1	Closed
4	×	1 00	2	Open
4	×	75	3	Closed
4	×	6	2	Closed
3 5	×	7	1	Closed
3 5	×	5	2	Closed
			39	

* These figures also demonstrate that the width of the anterior projection is not consequential to retention of implant An implant with a 5 mm wide projection remained in place as readily as one with a 3 5 mm wide projection The height of the projection nevertheless was critical in preventing closure of the anterior trephine hole A projection 1 mm or more in height always *prevented* tissue overgrowth and a projection less than 75 mm high always *permitted* overgrowth and closure

The *height* of the nubbin was the controlling factor A nubbin less than 75 mm above the anterior surface of the disc permitted overgrowth in nearly every case while anything higher arrested the tissue s progress Minute variations in height were critical

Pegs of tissue which grew into the peripheral skirt can be seen in Figure 9 an histological cross section of a cornea after the disc had been dissolved out Figure 10 (A & B) presents a high magnification of the connective tissue which invaded peripheral fenestrations and it is apparent that no epithelial cells continued with the tissue Figure 11 (A & B) shows the structure of the tissue at the edge of the anterior

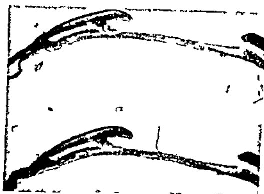
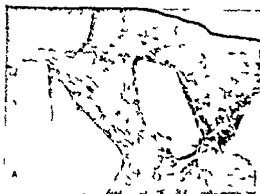


Fig 9 Photomicrograph of cross section of cornea after disc has been dissolved out Cut edge of anterior trephine hole and pegs of tissue which grew through peripheral fenestrations can be seen



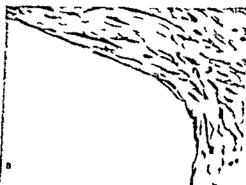


Fig 10 Photomicrograph showing connective tissue which invaded peripheral holes in skirt (A) Note that no epithelial cells grew through the holes (B)





Fig 11 Photomicrograph of corneal epithelial cells showing increase to 16-18 cell layer as they grow around the cut edge of anterior trephine hole (B) and reduction to 2-3 cell layer as they approach the area of proliferating connective tissue in region of fenestrations (A

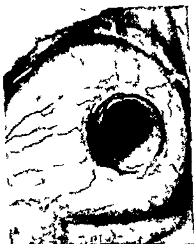
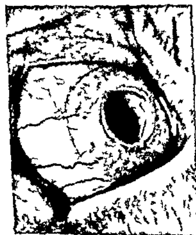
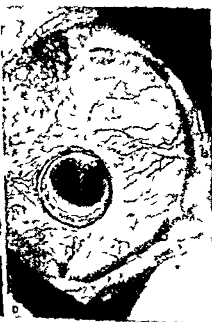




Fig 12 Rabbit corneas with plastic discs inserted intralamellarly with anterior trephine holes in place up to 4 years 3 months (to th natural death of the animal) A In place 4 years 3 months Rabbit #92 B In place 4 years Rabbit #19? C In place 3 years 10 months Rabbit #242 D In place 3 years Rabbit #221 F In place 2 years 9 months Rabbit #128







trephine hole The epithelial cells pyramid to approximately 16–18 cell layers in thickness as they come around the hole (Fig 11B) and immediately, in the posterior side of the anterior layer, they reduce to 2–3 cell layers in thickness and, as they approach the area of the proliferating connective tissue in the region of the peripheral holes, reduce to a one cell layer and then stop (Fig 11A)

A series of implants in rabbit corneas for up to four years and three months are shown in figure 12 Table V is a chart of the implants which have remained in place with patent anterior trephine holes to the natural death of the animal It is now felt that, barring infection (which seldom occurs in our animals), an implant placed as described will remain in place indefinitely with a patent anterior trephine hole

FABRICATION OF IMPLANT

We also found that each individual rabbit eye must be molded and the disc made to the exact conformation of the cornea or pressure necrosis and extrusion will result

Also, polishing materials cannot be used on the optical surfaces of the plastic corneas because microscopic bits of polishing materials will become embedded in the plastic, leading to foreign body reaction The optical surfaces must, therefore be molded to polished steel dies

CLARITY OF POSTERIOR SURFACE

In the majority of cases, if the procedure of lamellar dissection is accomplished with an operating microscope, posterior clarity will be realized if dissection is made down to Descemet's membrane and if Descemet s membrane itself is not too opaque

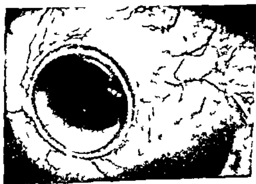


FIG 13 A crescent of opacification of the posterior corneal layer behind the anterior projection is visible This opacity was caused by malapproximation of the disc in the periphery The central portion remained clear

In figure 13 it is seen that the central portion where the plastic comes in contact with the back surface of the cornea remains perfectly transparent Where there was a slight peripheral malapproximation, fibroblastic tissue grew in and caused opacification, but the central portion remained clear

TABLE V — *Implants with anterior trephine holes patent to natural death of Rabbit*

Time Interval	*Rabbit #*	*Length of Time Open*
4 years and over (3 rabbits)	92	4 years 3 mos
	259	4 years
	192	4 years
3 years to 3 years 11 mos (4 rabbits)	247	3 years 10 mos
	210	3 years 1 mo
	145	3 years
	221	3 years
2½ years to 3 years (4 rabbits)	266	2 years 10 mos
	128	2 years 9 mos
	231	2 years 8 mos
	68	2 years 10 mos
2 years to 2½ years (4 rabbits)	280	2 years 3 mos
	82	2 years 3 mos
	83	2 years 3 mos
	167	2 years 2 mos
1½ years to 2 years (8 rabbits)	45	1 year 10 mos
	62	1 year 10 mos
	123	1 year 9 mos
	102	1 year 8 mos
	226	1 year 8 mos
	93	1 year 8 mos
	211	1 year 6 mos
	224	1 year 6 mos
1 year to 1½ years (8 rabbits)	225	1 year 5 mos
	69	1 year 3 mos
	202	1 year 3 mos
	227	1 year 2 mos
	85A	1 year 1 mo
	46	1 year
	101	1 year
	104	1 year
6 months to 1 year (15 rabbits)	154	11 mos
	113	11 mos
	196	11 mos
	87	10 mos
	206	10 mos
	201	10 mos
	81	10 mos
	269	10 mos
	163	9 mos
	198	9 mos
	271	9 mos
	164	8 mos
	73	7 mos
	66	7 mos
	100	7 mos

An implant (Fig 14) with a definite recess to provide space for fibrin to enter and to allow more fibroblastic proliferation was tested The posterior layer opacified



Fig 14 Disc with recess in posterior portion of central projection This created space for fibroblastic proliferation and caused posterior opacification

If there is good approximation between the posterior layer of the implant and the posterior layer of the cornea there will be no fibroblastic *proliferation* The transparency of the posterior portion of the graft depends upon the pressure which is exerted on the posterior layer by the back surface of the plastic

Therefore, it would seem that a *posterior trephine* hole will *not* be required in the majority of human cases and it will not be necessary to disturb the anterior chamber This will reduce the risk of infection and increased tolerance of the implant

When there is fibroblastic *proliferation or when Descemet's* membrane is opaque, a posterior trephine hole will be necessary This must be placed only when several months *post implantation*, tissue has grown into peripheral holes (anchoring the implant) and epithelium has grown around the anterior trephine hole (sealing off the anterior chamber from fluid loss and bacterial invasion)

Rabbits with the artificial corneas *implanted and anterior* trephine holes and posterior trephine holes open for varying periods are shown in figure 15 Figure 16 is an *histological cross section show*ing endothelium which grew around the edge of the posterior trephine hole to the area of the peripheral holes (where ingrowth of connective tissue had taken place) and stopped

If the posterior trephine hole stays patent for ten days, it will remain open indefinitely *It is necessary to heparinize the animal to* prevent the precipitation of fibrin in the posterior trephine hole If this is averted, a matrix *will not be laid down for the overgrowth of* connective tissue



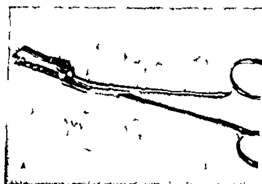
FIG 15 Rabbit corneas with plastic discs and central anterior and posterior trephine holes A The anterior trephine hole remained open 2 years 10 months the posterior trephine hole remained open 2 years 5 months to th natural death of the animal (Rabbit #68) B The anterior trephine hole remained open 2 years 3 months 14 days the posterior trephine hole remained open for 1 year 10 months 22 days to the natural death of the animal (Rabbit #83) C The anterior trephine hole remained open for 1 year 3 months the posterior trephine hole remained open 1 year 10 days to the natural death of the animal (Rabbit #69) D The anterior trephine hole remained open for 1 year 25 days the posterior trephine hole remained open for 9 months 27 days to the natural death of the animal (Rabbit #104) Traumatic cataract is visible through the posterior opening E Anterior trephine hole remained open for 1 year 4 days posterior trephine hole remained open for 9 months 4 days to the natural death of the animal (Rabbit #46)

TREPHINE INSTRUMENT

An instrument was designed to cut the posterior trephine hole (Fig 17 A & B) It consists of a circular cutting blade motivated by a series of watch gears which are turned by a knob from the outside The lower arm of the instrument goes behind the plastic after an



Fig 16 Photomicrograph of posterior trephine hole in posterior layer of rabbit cornea showing endothelial cells migrating around cut edge and stopping at fibroblastic tissue proliferating into peripheral holes



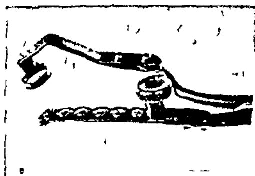


Fig 17 A Instrument used for cutting trephine hole in rabbit cornea posterior to plastic disc a month or more after implantation B Enlargement shows trephine cutting blade which is placed in the anterior chamber through incision at edge of disc It is motivated remotely by a knurled knob through a series of watch gears The one month period between original operation and posterior trephine procedure permits sealing of wound by fibroblastic tissue and epithelium and prevents bacterial invasion and leakage of aqueous

incision at the edge of the disc and the upper arm goes in front of the plastic The blade is then rotated by turning the knurled knob on the outside Figure 15E is a posterior trephine hole seen from an oblique angle so that the cut edge of the hole is visible

IMPLANT MATERIAL

Figure 18 is the formula for the conversion of methyl methacrylate monomer to methyl methacrylate polymer Incompletely purified and non standardized methyl methacrylate produced varying results in different animals, some of the plastic produced severe reactions and some minimal reaction In different batches from the same manu facturer there was variation Inconsistent results were even obtained from different sections of the same plastic rod

The results were dependent upon the amount of trace impurities in the material the amount of accelerator, inhibitor etc which was present and whether or not pre polymerization had taken place Hydroquinone a common inhibitor, produces a severe reaction in the cornea of rabbits

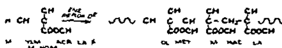


FIG 18 Polymerization reaction of methyl methacrylate with benzoyl peroxide as accelerator If in completely poly merized monomer produces severe re action when implan ted in cornea

Because impurities and additives are present in commercial methacrylate we have had to purify our own monomer and standardize polymerization in order to get consistent results

As an aside here, it is felt that many of the reactions which have occurred with plastics placed in the anterior chamber to replace catar actous lenses have been a result of poor purification and standardization of the plastics which were used

At the present time we are investigating the synthesis of a new type of plastic which is hydrophilic which permits absorption and transference of water through its matrix to approximately 40–70% of its weight and has a high diffusion coefficient for oxygen and CO_2 (Fig 19) This by the way should be more physiological than methyl methacrylate and will produce even better results

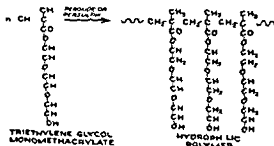


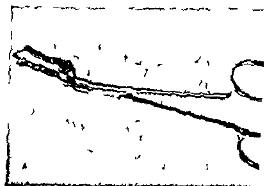
FIG 19 Synthesis of hy drophilic polymer which permits ab sorption of water and transf rence through its matrix to approximately 40–70% by weight It has a high diffusion coefficient for oxy gen and CO Ex perimental work is being done with this at the present time in the Ophthalmic Plastics Laboratory

TREPHINE INSTRUMENT

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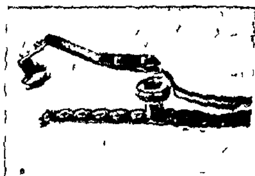


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incision at the edge of the disc and the upper arm goes in front of the plastic The blade is then rotated by turning the knurled knob on the outside Figure 15F is a posterior trephine hole seen from an oblique angle so that the cut edge of the hole is visible

sarcomata and cancers In general a high rate of remission was obtained and the unpleasant symptoms of malignant disease have been relieved Some authors have reported good results lasting over three years

If I ever wanted to help my patients I had no other choice than the chemotherapy for the disease of my patients were bilateral cancer metastases of the eyes which at least in one patient identical with other proved metastases in her body

What could have been more useful in these two cases — to operate or give an X Ray treatment?

The first case concerned 35 year old woman who had been referred to me by a colleague on the 23rd of April 1960 (more than 2½ years ago) because of a rapidly developing detachment of retina in her right eye Examination showed a white infiltration of the whole central area of "Choroid" with a slight detachment of *retina in the* upper nasal quadrant Its surroundings showed some grey white areas with a prominence upto 3 D no haemorrhages nor any signs of inflammation were seen in the retina The corrected vision was 0 6 the picture was that of a metastatic carcinoma The diagnosis being based on the fact that she had had a histologically verified carcinoma removed 2½ years previously followed after 2 years by lymphatic recurrences of the same histological nature which had been removed and radiational treatment given

The patient, who was *very cachectic refused* treatment with Endoxan but shortly thereafter developed a similar metastases in the left eye Visual acuity sank to R E 0 1 and L E 0 3 Treatment with Endoxan 100 to 200 mgm every second day intravenously was commenced however she lost weight, ran a temperature while the, *leucocytic count fell from 5,000 to 1 270 The treatment* was therefore stopped Her general condition rapidly recovered and ten weeks later she left the hospital. The tumours had disappeared from both *eyes* leaving greyish white pigmented areas and the visual acuity in each eye was normal Since she left the hospital she has received ten injections of Endoxan intravenous at two day intervals and one or two tablets of Endoxan or Mitarson (0 5 gr) daily by mouth her blood count being periodically checked Now 2½ years later she is well full of energy and at work There is no recurrence of the original tumour or metastases and the vision is normal How long this will last is of course unknown

The second case concerns of sixty year old and stout woman who had a radical mastectomy for histologically verified carcinoma Since then she had several radiational treatments as a precaution and seemed to have been cured *Suddenly* two years ago, she developed bilateral proptosis with diplopia X Rays showed neoplastic metastases in the skull Daily *intravenous* injections (200 mgm) of Endoxan were given In the following ten days *the leucocytic* count fell from 8 800 to 5 000 The exophthalmos was *less and* the diplopia had disappeared For a

CHEMOTHERAPY OF OCULO ORBITAL CARCINOMATOUS METASTASES

PROF DR HANS SCHMELZER

(*Bamberg*)

The question of chemotherapy of malignant tumours is still very much in dispute, but *is increasing in significance* year by year Even a scientist as Prof H K Bauer, Heidelberg, says that we are only able to cure about 18% of all cases of cancer by operation and X Ray treatment with a follow up period of at least five years It follows that the importance of chemotherapy must be recognised

I do not wish to enter into the local therapy of malignant tumours as recommended by *Domagk, after which a special kind of "Loststoff"* (E 39 " Bayer ") is injected into the surroundings of malignant tumours On this subject, Pillat and others in many countries have already reported, nor do I wish to discuss the method by *Schliephake* of irra diation of the hypophysial hypothalmic system with which he was able to stop or control the growth of malignant tumours in more than eighty patients, so that several of them were able to work again

I will, however, report on two patients on whom I obtained extremely good results upto the present by the intravenous injection of the cytostatic " Endoxan " The first was a case of bilateral metas tatic carcinoma of the choroid (with secondary serous detachment) which occurred after surgical and X Ray treatment of a cancer of a breast, the second case showed a rapidly increasing bilateral exophthalmus due to retrobulbar metastatic carcinomata which also occurred after an amputation and X Ray treatment of a cancer of the breast some years previously

The ideal chemotherapy depends on the elaboration of a cancero toxic substance, active at the site of the growing tumour of sufficient selectivity that it affects as few as possible of the body cells and only restrains the growth of *neoplastic cells This is the fundamental pro* blem on which cytostatic have hitherto failed as for instance the Athylenimminchinon *of Domagks E 39 soluble and substance No* 3231 that *Liegl* used on a case similar to mine a year ago

A number of *publications have appeared about the effect of* Endoxan therapy on all kinds of malignant tumours and blood diseases Some of these publications sound rather pessimistic One author even stated that in the field of chemotherapy our knowledge is still at the " ice age stage ' Others again report good results, especially lymphatic (not myeloid) Leukaemia, Hodgkins disease and a number of

sarcomata and cancers In general a high rate of remission was obtained and the unpleasant symptoms of malignant disease have been relieved Some authors have reported good results lasting over three years

If I ever wanted to help my patients I had no other choice than the chemotherapy, for the disease of my patients were bilateral cancer metastases of the eyes which at least in one patient identical with other proved metastases in her body

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The patient who was very cachectic, refused treatment with Endoxan but shortly thereafter developed a similar metastases in the left eye Visual acuity sank to R E 0 1 and L E 0 3 Treatment with Endoxan 100 to 200 mgm every second day intravenously was commenced however she lost weight, ran a temperature while the, leucocytic count fell from 5 000 to 1,270 The treatment was therefore stopped Her general condition rapidly recovered and ten weeks later she left the hospital The tumours had disappeared from both eyes leaving greyish white pigmented areas and the visual acuity in each eye was normal Since she left the hospital she has received ten injections of Endoxan intravenous at two day intervals and one or two tablets of Endoxan or Mitarson (0 5 gr) daily by mouth her blood count being periodically checked Now 2½ years later she is well full of energy and at work There is no recurrence of the original tumour or metastases and the vision is normal How long this will last is of course unknown

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further two weeks, the intravenous injections were given every second day Altogether the patient was given 9 8 G of Endoxan intravenously and in the intermediate periods 1 to 2 tablets of Endoxan by mouth daily

She maintained her treatment for over one year and then allowed it to lapse Thereupon, the exophthalmos recurred, to disappear, however, with further injections of Endoxan, the leucocytes meantime falling from 7,200 to 3,100 The patient remained well until four weeks ago, when she complained of pains in her back X-Ray examination revealed two metastases in the vertebral column in the lumbar region After approximately three weeks and half of clinical treatment with Endoxan as well as a 'blood transfusion' and Anabolite the patient had recovered so far that she could walk again by herself and we could send her home On the X Ray taken on the day she left the hospital one can clearly recognise the beginning of "Ossification" of the destroyed part of the bones as a sign of regeneration How long, however, this will last is questionable

This case of multiple metastases — among them two retrobulbar occurring eleven years after an initial operation and subsequent radiational treatment shows how well and rapidly these malignant tumours respond to Endoxan

The question arises whether these recurrences could have been prevented if one had immediately supplemented the operative and radiological treatment with Endoxan treatment or other form of chemotherapy?

I consider the communication of these cases important because each of us may be asked to help in such desperate cases Further, operation is without any prospect and the X Ray treatment very problematical in its results

The result with the Endoxan treatment I obtained so far with my patients provides a possibility to help even if it is only temporary

I hope to inform you of the further development of these two cases at a later date

EXPERIMENTAL AND CLINICAL RESEARCH ON RIGIDITY OF THE EYE

NESTEROV, A P (*Kuibyshev*)

Experimental investigations were carried out on 26 enucleated eyes For the measurement of the ophthalmotonus a set of Maklakov s applanation tonometers was used, with weight of 5, 10 15 and 20 grams and an impression tonometer of the Schiotz s type

The changes in ophthalmotonus initiated by the application of a tonometer to the eye were registered simultaneously by means of a highly sensitive electronic manometer connected with a registering potentiometer

The data thus received were compared with the results of a clinical research on rigidity, carried out by means of a set of Maklakov s applanation tonometers on 203 eyes and with the help of Schiotz s electronic tonometer on 145 eyes

When applanation tonometers were used the coefficient of rigidity constituted in average 0 0186 (0 0080 to 0 0410), and the average value of elasto rise (after S F Kalfa) was 9 7 ± 4 3 mm of Hg The Schiotz s tonometer gave slightly bigger values of the coefficient of rigidity which on 145 eyes equalled to 0,0239 ± 0 0138

The coefficient of rigidity as well as the ' elasto rise changes along with alteration of the ophthalmotonus level

The author suggests to use the conception of standardised elasto rise By this term one understands the difference (in mm of Hg) between the readings of two tonometers of different weight applied to an eye with the average value of ophthalmotonus (16 mm of Hg)

An interpolation formula is suggested for standardising The relation between standardized elasto rise and rigidity of an eye is still being discussed

CONJUGATED ESTROGEN IN PROPHYLAXIS OF SECONDARY HYPHEMA

J G GILLAN

Presented at the International Congress of Ophthalmology
New Delhi — December 1962

(Read by Dr P K Basu, at the Author's request)

The present article is the third of a series of studies conducted by the author in an effort to discover and reduce the number of secondary haemorrhages following direct and non penetrating injury to the eye Because haemorrhage into the anterior chamber can be checked so easily and quickly, this was chosen as a good guide from the clinical point of view

In the first article [1] an effort was made to study the complications associated with hyphema and the medical treatment An introduction to the use of conjugated estrogen was made

In the second article, 70 cases of hyphema treated by the author were analyzed [2] In this 35 cases were treated conservatively and 35 by the use of conjugated estrogen A considerable reduction in the incidence of secondary haemorrhage was noted in those cases treated with the conjugated estrogen

This series has now been increased to 85, in which the 35 previously described as controls were again used as controls while those cases having conjugated estrogen were divided into 15 which had oral preparation and 35 which had *intravenous administration* of the hormone The clinical results are summarised in the attached table

Clinical Results	*No of Cases*	*Sec Haem*	*Sec Glaucoma*	*Visual Loss*
I Conservative Medical Therapy Alone	35	9	4	3
II Conservative Care Plus Oral Estrogen	15	1	1	1
III Conservative Care Plus I V Estrogen	35	1	0	1

The cases having oral estrogen had Premarin tablets 1 25 mg given three times a day during their stay in hospital with hyphema Those treated with intravenou estrogen had the clinical dose of 20 mg given intravenously on admission and in certain cases where haemorrhage might be imminent another intravenous dose as required The present treatment which is being used is to give 20 mg intravenously on admission A similar dose on the third day and a similar dose on the fifth day if the hyphema has not completely subsided In children where this intravenous administration is too difficult, intramuscular Premarin can be given of 10 or more milligrams each dose

INVESTIGATION OF ACTION

In view of the clinical benefit in preventing secondary haemorrhage an effort was made to study the action of the conjugated estrogen in human subjects Schiff and Burn[3] had discovered that conjugated estrogen given to hamsters intravenously, could produce a marked change in the ground substance of blood vessels It therefore seemed feasible that similar changes should be possible to demonstrate in humans A simple experiment therefore, was devised During cataract surgery the author normally does a peritomy prior to making a corneo scleral section It was therefore perfectly easy to remove a small piece of conjunctiva at the first operation

Three groups of cases were examined Six patients were operated upon seven to eight days after the first cataract extraction and during this period they were given oral Premarin at 1 25 mg three times a day The conjunctiva taken from the eye at the second operation showed no difference in the ground substance of the blood vessels from those found in the first case The second consisted of two cases in which 20 mg of estrogen was given intravenously, twelve and thirteen hours ahead of the operation The third consisted of four cases in which conjugated estrogen was given in the dose of 20 mg one hour before the operation Using Toluidin Blue and Colloidal Iron for stains it was not possible to demonstrate by ordinary histological means any difference in the ground substance of the specimen taken from the first eye and that from the second eye after conjugated estrogen

It should be pointed out however that the dose given in these cases was the ordinary dose used in prophylaxis A proportionate dose in an adult compared to the dose given by Schiff and Burn to their hamsters would require 50 to 60 mg of intravenous Premarin being used Schiff and Burn also found that their time of maximum change was three hours after the administration of the conjugated estrogen

DISCUSSION OF CLINICAL RESULTS

It should be noted from the series that while the incidence of secondary haemorrhage was greatly reduced as a result of the use of conjugated estrogen this dread complication was not completely abolished However it is interesting to note that both those cases,

where secondary haemorrhage occurred, arose from injuries inflicted in the limbal area

Drs Brodin and Fox, in the Round Table discussion on *haemostasis*[4] *noted that* intravenous conjugated estrogen was beneficial in the treatment of oozing from an adenoid layer, but it was of much less value for a tonsil bed where ligatures were necessary It therefore appears that intravenous use of conjugated estrogen is not likely to be so effective where the larger blood vessels of the ciliary body are torn, as in the trauma to the small vessels on the iris

In the second article, written by the author, the idea was proposed that secondary haemorrhage possibly occurred in individuals where the body's own conjugated estrogen or physiological haemostatic agent was deficient One of the reasons for believing this was that when a case had developed secondary haemorrhage after the original trauma, they frequently also developed secondary haemorrhage after any subsequent surgical intervention Unfortunately, no test has yet been devised, at present, which can quickly determine whether there is any deficiency of the body's own estrogen level It is possible that later we will be able to distinguish those cases which will develop *secondary haemorrhage, from those cases which will not* When that day comes, it will be possible to administer a prophylactic dose of estrogen in a scientific manner and with the same confidence which we would have in treating any deficiency disease

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3 Schiff M and Burn H F 1961 The Effect of Intravenous Estrogens on Ground Substance *Arch Ophth*, **73** 43

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RADIOSULFATE RETENTION IN ORBITAL TISSUES RELATIONSHIP TO THYROTROPIC EXOPHTHALMOS *†

HESKEL M HADDAD, M D ‡

The orbital tissues of the guinea pig and in particular the Harderian gland respond to thyrotropic hormone (TSH) administered to the animal by an increase in size This induces proptosis [1-6] In addition an augmentation of mucopolysaccharide synthesis [5-6] is suggested by the increase in the 24 hour uptake of radiosulfate [7 10] The latter phenomenon offers a bioassay method for TSH like effect of sera of patients with endocrine exophthalmos However for an adequate response an optimal dose of 1 unit of TSH per animal per day for two days is necessary [10]

In the present study the sensitivity of the sulfate uptake of the Harderian gland in response to TSH is increased by using a 72 hour uptake (which will be called retention) instead of a 24 hour uptake Using such a method the sera of 12 patients with endocrine exophthalmos are qualitatively assayed for TSH like effect

METHODS

Young female guinea pigs, in groups of 6 animals per experiment, were given carrier free S^{35}—labled Na_2So_4* intraperitoneally Thyrotropic hormone (TSH)† or serum in 0 5 ml saline solution was injected intraperitoneally simultaneously with the radiosulfate and daily thereafter for 2 days Seventy two hours after radiosulfate injection the animals were sacrificed The orbital tissues and in particular the Harderian gland and the thyroid gland were dissected cleaned of adventitia weighed hydrolyzed and counted individually in a Packard Tri Carb liquid Scintillation counter

The results (in counts/minute/mg of wet weight of tissue) were compared statistically using the t test (11) For this presentation,

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† Supported by Grant A 5 03 U S Public Health Service National Institute of Arthritis and Metabolic Diseases National Institutes of Health Bethesda Md

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‡ Special Fellow National Institute of Neurological Diseases and Blindness National Institutes of Health Bethesda Maryland Present address The Mount Sinai Hospital New York N Y

* S^{35} labled Na_2So_4 was purchased from Abbott Laboratories Oak Ridge Tennessee

† TSH was used as the commercial preparation Thytropar some purchased and some generously given by the Armor Laboratories.

however, the response of the tissue's radiosulfate was expressed as per cent of the control group for each experiment Using percentage figures, a significant response was found to lie roughly above a 12–15% increase in radiosulfate uptake

MATERIAL

Sera of 12 patients with endocrine exophthalmos (22–63 years old) were assayed using 0 1–0 2 ml of serum daily for 3 days per animal The assay was made against a control group of animals injected with normal saline only, a group given TSH and a third group treated with sera obtained from euthyroid controls For the latter purpose sera of 13 euthyroid controls (18–70 years old) were used individually or pooled

Of the 12 patients, at the time of blood collection, 5 had inactive and 7 had progressive endocrine exophthalmos Four of the patients were in hypothyroid state

RESULTS

TSH EFFECT Radiosulfate retention (72 hours uptake) by the Harderian gland of the guinea pig was highly responsive to TSH at as low a dose as 0 1 unit per day × 3 Even though there was considerable variation in the response from one experiment to the other, the increase in the Harderian gland's radioactivity ranged between 24 and 56% of the controls The thyroid gland of the guinea pig responded significantly to TSH by an average increase in the radiosulfate retention by the gland of 34% of the control A dose response curve is plotted on log log coordinates (Fig 1)

SERUM EFFECT Whereas there was very little variation in the response of the 72 hour radiosulfate retention by either the Harderian or the thyroid glands to different individual or pooled sera of euthyroid

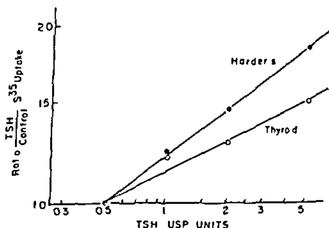


FIG 1 Dose Response curve of TSH (in USP units) and the radiosulfate uptake by the Harderian and the thyroid glands (in fractions of normalized controls) plotted on log log coordinates

controls as compared to each other or to normal saline the sera of patients with endocrine exophthalmos behaved differently Of the 7 patients with progressive exophthalmos (Table 1) sera of 6 augmented the sulfation of the Harderian gland significantly (19–45%) and one serum showed no effect Of the 5 patients with inactive exophthalmos on the other hand 2 sera caused no stimulation of Harderian gland sulfation 2 sera each induced 11% increase in the gland s radiosulfate and the fifth serum augmented sulfation significantly by 20% above the control

The response of the thyroid gland of the guinea pig to the patients sera did not follow specifically the activity or inactivity of the exoph thalmos Interestingly enough the response varied according to the thyroid status of the patient namely whether the patient was euthyroid or hypothyroid As seen in Table 1 there was significant augmentation of thyroid sulfation by the sera of the four patients who were hypo thyroid ranging between 15 and 41% of the control Of the other 8 euthyroid patients there was an apparent diminution in the gland s radiosulfate induced by sera of 4 patients whereas an insignificant increase (4–12%) was induced by the sera of the rest

TABLE 1

		Age Years	Sex	P B I mcg/100 ml	% deviation from control of S^{35} uptake Harderian gland Thyroid gland	
					Harder	Thyroid
I	*Progressive Exophthalmos Euthyroid Status*					
1	J L.*	63	M	7 2	+ 27	− 23
2	C K †	49	F	5 0	+ 45	+ 11
3	C McK	37	F	6 0	+ 0	− 23
II	*Progressive Exophthalmos Hypothyroid Status*					
4	H P *	42	F	4 1	+ 17	+ 15
5	E D	22	F	4 1	+ 27	+ 29
6	T D ‡	62	M	3 3	+ 19	+ 16
7	J W	45	F	4 0	+ 37	+ 41
III	*Inactive Exophthalmos Euthyroid Status*					
8	B R	36	F	8 1	+ 11	− 14
9	M M	49	F	8 0	+ 11	+ 4
10	O S	58	M	6 1	− 7	− 8
11	F F	50	M	4 9	+ 20	+ 12
12	H W **	55	F	6 4	− 1	+ 4

Unilateral exophthalmos both of the right eye

† The radiosulfate uptake by the Harderian gland increased from 21% to 45% above control within a period of 3 months during which her exophthalmos became remarkably worse

‡ Exophthalmos developed almost simultaneously with thyrotoxicosis Patient was decompressed unilaterally biopsy was read as pseudotumor Exophthalmos responded to steroid therapy

** Exophthalmos regressed

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RESULTS

TSH EFFECT Radiosulfate retention (72 hours uptake) by the Harderian gland of the guinea pig was highly responsive to TSH at as low a dose as 0 1 unit per day × 3 Even though there was considerable variation in the response from one experiment to the other, the increase in the Harderian gland s radioactivity ranged between 24 and 56% of the controls The thyroid gland of the guinea pig responded significantly to TSH by an average increase in the radiosulfate retention by the gland of 34% of the control A dose response curve is plotted on log log coordinates (Fig 1)

SERUM EFFECT Whereas there was very little variation in the response of the 72 hour radiosulfate retention by either the Harderian or the thyroid glands to different individual or pooled sera of euthyroid

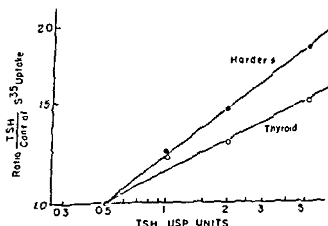


FIG 1 Dose Response curve of TSH (in USP units) and the radiosulfate uptake by the Harderian and the thyroid glands (in fractions of normalized controls) plotted on log log coordinates

controls as compared to each other or to normal saline the sera of patients with endocrine exophthalmos behaved differently Of the 7 patients with progressive exophthalmos (Table 1) sera of 6 augmented the sulfation of the Harderian gland significantly (19–45%) and one serum showed no effect Of the 5 patients with inactive exophthalmos on the other hand 2 sera caused no stimulation of Harderian gland sulfation 2 sera each induced 11% increase in the gland s radiosulfate and the fifth serum augmented sulfation significantly by 20% above the control

The response of the thyroid gland of the guinea pig to the patients sera did not follow specifically the activity or inactivity of the exophthalmos Interestingly enough the response varied according to the *thyroid status of the patient namely whether the patient was euthyroid* or hypothyroid As seen in Table 1 there was significant augmentation of thyroid sulfation by the sera of the four patients who were hypothyroid ranging between 15 and 41% of the control Of the other 8 euthyroid patients there was an apparent diminution in the gland s radiosulfate induced by sera of 4 patients, whereas an insignificant increase (4–12%) was induced by the sera of the rest

TABLE I

		Age Years	Sex	P B I mcg/100 ml	% deviation from control of S^{35} uptake Harderian gland Thyroid gland	
					Harder	Thyroid
I	*Progressive Exophthalmos Euthyroid Status*					
1	J L.*	63	M	7 2	+27	−23
2	C K.†	49	F	5 0	+45	+11
3	C McK	37	F	6 0	+ 0	−23
II	*Progressive Exophthalmos Hypothyroid Status*					
4	H P *	42	F	4 1	+17	+15
5	E D	22	F	4 1	+27	+29
6	T D ‡	6?	M	3 3	+19	+16
7	J W	45	F	4 0	+37	+41
III	*Inactive Exophthalmos Euthyroid Status*					
8	B R	36	F	8 1	+11	−14
9	M M	49	F	8 0	+11	+ 4
10	O S	58	M	6 1	− 7	− 8
11	E F	50	M	4 9	+20	+12
12	H W **	55	F	6 4	− 1	+ 4

* Unilateral exophthalmos both of the right eye

† The radiosulfate uptake by the Harderian gland increased from 21 % to 45% above control within a period of 3 months during which her exophthalmos became remarkably worse

‡ Exophthalmos developed almost simultaneously with thyrotoxicosis Patient was decompressed unilaterally biopsy was read as *pseudotumor* Exophthalmos responded to steroid therapy

** Exophthalmos regressed

DISCUSSION

The stimulating effect of TSH on the Harderian gland of the guinea pig was found to increase the 24 hour radiosulfate uptake by this gland but only in doses of 1 unit per day for 2 days (10) In order to devise a bioassay method for TSH-like effect based on such response, the sensitivity of the response had to be increased several folds Direct tissue paper chromatograms demonstrated that a large percentage of the radiosulfate in the gland at 24 hours remained in its inorganic form The possibility that the increase in the gland's radiosulfate in response to TSH was mainly in the organic sulfate fraction was recently corroborated by *Brunish* (12) Since our study depends practically on direct tissue assay of radioactivity, the elimination of the inorganic radiosulfate fraction by dialysis or other physical means would be impractical Using direct tissue chromatography as an index, however it was found that by allowing the administered radiosulfate to remain in the animal about one biological half life (about 72 hours) prior to killing, almost all the inorganic radiosulfate fraction in the Harderian gland disappeared Thus the method of study was modified from a 24 hour uptake to a 72 hour "retention" of radiosulfate by the Harderian gland of the guinea pig

The response of both the Harderian and the thyroid glands to TSH were improved several folds using a 72 hour uptake of radiosulfate As seen in Fig 1 this response had the potentiality for a bioassay method for TSH like effect

The response of the Harderian gland to the sera of patients with endocrine exophthalmos demonstrated the utility of this response as at least a qualitative bioassay method

The response of the thyroid gland of the guinea pig to the sera of patients with endocrine exophthalmos correlated with the clinical (hypothyroidism and myxedema), and biochemical (serum PBI and cholesterol) status This pointed to a dissociation in the response of the two tissues of the guinea pig to patient s sera versus TSH It further suggested that commercial TSH had an additional factor which stimulated the orbital tissues of the guinea pig as has already been pointed out by other observers (13–14) But most important was the suggestion that a humoral factor existed in patients with endocrine exophthalmos which stimulated only the orbital tissue of the guinea pig even when no evidence for increased circulating TSH was elicited The nature of this factor is yet to be determined It may however, be assayed qualitatively at least, using the Harderian gland s 72 hour retention of radiosulfate as an index Quantitative bioassay would remain difficult until the exact nature of this factor and its actual influence on guinea pig orbital tissue are determined unequivocally

SUMMARY

Using 72 hour radiosulfate uptake (retention) the Harderian and the thyroid glands of the guinea pig responded to as little as 0 1 unit of TSH per day administered for three days to the animal Using this response as an index sera of 12 patients

with endocrine exophthalmos were assayed Sera of 6 out of 7 of the patients with progressive exophthalmos induced significant increases in the Harderian radiosulfate whereas the serum of only one out of 5 of the patients with inactive exophthalmos caused a similar response The response of the thyroid gland to these sera indicated a dissociation in the response of the two tissues since the thyroid response depended on the titer of circulating TSH as evidenced by clinical and biochemical criteria

ACKNOWLEDGEMENT

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be treated, and finally a stage where certain types of cases are treated even although degenerative changes are absent or invisible

The following have reported on the treatment of retinal holes Sabbadini (1934) Amsler (1938), Fleischer (1947) Weber (1947), Franceschetti and Balavoine (1949), Custodis (1950), Sedan Bauby (1950) Schepens (1950 1952), Safar (1953), Meyer Schwickerath (1956) Amiga (1958), Berliner (1958) Arruga (1958) Dollfuss (1958), Schepens (1958) Shapland (1958), Callahan (1958) Hruby (1958), Jess (1958), Amsler (1959) Bietti (1959), Schiff Wertheimer and Paufique (1959), Safar (1959) Franceschetti and Maeder (1959), Lindner (1959) Meyer Schwickerath (1959), Pischel (1959), Weve (1959) Lincoff (1961) These authors differ among themselves with regards to insistence on which holes to close Among the more conservative are Berliner Bietti Dollfuss, Safar Schiff Wertheimer and Paufique, and Schepens The following factors were by most authors considered decisive The age of the hole and its tendency to heal its size form and position whether single or multiple the presence of vitreous attachment in the neighbourhood, the refraction of the eye, the presence of a history of detachment in the fellow eye the age temperament and occupation of the patient and a family history of detachment Complaints of flashes are usually significant

The treatment of degenerative areas has been described by Weber (1947) Franceschetti (1955) Arruga (1958), Dollfuss (1958) Callahan (1958) Jess (1958) Amsler (1959) Lindner (1959), Sabbadini (1959), Schiff Wertheimer and Paufique (1959) Maeder (1959), Meyer Schwickerath (1959) (1515 cases) Pischel (1959) *Weve* (1959), Custodis (1960) (757 cases) and Lincoff (1961) Factors to be considered before deciding on treatment for degenerative areas are their extent situation and progressive nature, their presence in second eyes the imminence of cataract extraction especially in myopia the youth of the patient and complaints of flashes Most *surgeons are* conservative regarding the treatment of degenerative areas and confine themselves to those where there is vitreous pull Heinzen (1960) *divides* the changes which may require treatment into five groups Pigment verschiebung, cobblestones rosettes pallisades and nail tracks

There is finally the group of cases in which prophylactic treatment is frequently carried out even in the absence or near absence of degeneration These include cataract extraction in *second* eyes , in high myopia, or in cases such as Marfan s syndrome, where there is a danger of vitreous loss (Schiff Wertheimer 1958 Mylius 1959 Paufique and Spira 1959 Klott, 1961 Lincoff 1961)

Heinzen (1960) in discussing the need for preventive measures compares the risk of photocoagulation (1% out of 1 000 treated cases developed retinal detachment in the series reported by Meyer Schwickerath 1959) with the probability of detachment occurring after spontaneous hole *formation* Regarding this latter probability there is much difference of opinion Colyear and Pischel (1956) found that detachment followed in 20% of retinal holes *On the other* hand

A NATIONAL COOPERATIVE STUDY IN THE PREVENTION OF RETINAL DETACHMENT—A PRELIMINARY REPORT

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Although there is now a high possibility of successfully treating a detachment of the retina, failures in most clinics are still between 20 30% and in the best of cases there are months of cumbersome invalidity Preventive measures are, therefore, important and the purpose of this communication is to assess the effectiveness of this as shown in a national cooperative study being carried out in Israel since 1960

Prophylactic treatment of detachment of the retina consists of therapy applied to a retinal lesion before there is actual detachment Included in these lesions are retinal tears where the lid only is lifted into the vitreous

The possibility of preventive treatment of retinal detachment is based on three circumstances

(*a*) In the majority of cases of idiopathic retinal detachment the detachment retinopathy goes through a phase of predetachment changes

(*b*) Photocoagulation by means of the apparatus designed by Meyer Schwickerath provides a relatively easy and safe alternative to diathermy in the treatment of the predetachment phase, although in many cases diathermy is the more suitable method

(*c*) Refined methods of ophthalmoscopy make it possible to visualise with ease the fundal changes in the pre detachment phase

Theoretically it is possible to prevent the majority of retinal detachments by means of the discovery and treatment of the pre-detachment phase in all potential cases

The history of the prophylactic treatment of retinal detachment can be divided into three stages A stage where the prophylaxis was confined to retinal holes and involved a discussion as to which holes should be closed, a later stage, where prophylaxis extended to the treatment of the pre hole retinal degenerative changes and included discussion of the circumstances under which certain changes should

(A) The factors initiating the degenerative stage are situated presumably in either the choriocapillaris or in the vitreous, or in both simultaneously There is histological evidence for each of these factors Okun has shown that obliteration of the choriocapillaris may be associated with cystoid degeneration and pigment loss On the other hand vitreo retinal adhesions seem capable of giving rise to cystoid changes and disturbances in the retina (Fig 1 and 2) It has been suggested that the pull of a vitreous adhesion gives rise to cystoid changes and thereafter the continuation of the pull converts the cystoid change into a hole The histological findings in a case previously reported to the Congress suggest that changes in the choriocapillaris and vitreous may contemporarily produce the retinal degenerative changes It is not likely that clinical observations will finally determine the nature of the initiating factor except in a small minority of cases The clinical presence of vitreous pull does not obviate the possibility of an initiating choroidal factor and the clinical absence of vitreous pull does not prove that it was not at one time present (Fig 3) The evidence regarding the nature of the initiating factor will then probably be microscopic rather than clinical in nature and therefore is not likely to accrue from the clinical studies which are the subject of this report

(B) On the other hand the temporal relationship of the details of the degenerative stage may well be studied clinically and the relationship of pigment proliferation cystoid degeneration snail tracks palisade formation and vascular sclerosis be determined The role of the vitreous pull in a final factor in the hole formation is accepted, but there is not yet commonly accepted evidence regarding the type of retinal degeneration which is ominous of hole formation, and if so to which type of hole or whether indeed retinal degeneration must always be clinically present

(C) Finally it should be possible to determine by planned clinical study which type of hole most frequently gives rise to detachment and the time it may take to do so

The problems may be stated tabularly as follows —

(A) *Initiating Sequence*	(B) *Degeneration hole Sequence*	(C) *Hole-detachment Sequence*	
Vitreous Pull or Choriocapillaris Occlusion or both	Pigmentation Cystoid—Degeneration Snail tracks Lattice—Formation Vascular—Sclerosis	Circular Hole Horse shoe hole	Retinal Detachment No Retinal Detachment

Adams (1956), Teng and Chi (1957), and Okun (1961), found the occurrence of holes in so called normal eyes far beyond what the incidence of retinal detachment might lead to expect There is, as can be easily understood, even greater unpredictability of prognosis in many types of retinal degeneration with regards to the likelihood of a supervening hole formation

There are three main problems in the preventive treatment of retinal detachment, all of which have in only a certain measure been solved by the authors whose works have been quoted

(a) How can eyes with pre detachment changes be discovered Some cases, probably most, have symptoms of muscae or flashes at one time or another, yet there are many cases where those are slight or do not drive the patient to the oculist, or their implication not appreciated by the examiner

(b) How can it be statistically proved that retinal detachment has been prevented by prophylactic measures

(c) What is the natural history of the pre detachment phase What retinal, choroidal or vitreal changes or combination of changes proceed to hole formation, and which holes lead to retinal detachment

REQUIREMENTS AND POSSIBILITIES

The discovery, in large numbers, of cases with pre detachment retinopathy is dependent on the setting up of special retinal clinics in each department where patients with symptoms suggestive of the retinopathy may be examined by ophthalmoscopists specially experienced in the necessary techniques and with plenty of time to do so In addition groups of cases have to be specially invited and examined in which the expected incidence of retinal detachment is relatively high As will be seen later the invited groups in Israel are "second eyes" and "aphakic myopes"

Statistical proof of the efficacy of preventive measures depends on the consideration of the incidence of retinal detachment throughout a confined geographical area during a number of years and the effect on this incidence of a known number of prophylactic measures In this way it will be possible to determine if expected incidence has been diminished as the result of stated preventive measures It will not be possible to answer this problem if patients go to different ophthalmologists for diagnosis, preventive measures or perhaps a subsequent detachment and these ophthalmologists are not in a position to pool their findings Briefly, the statistical proof of the efficacy of preventive measures depends on these measures and the incidence of detachment being made notifiable

The pre detachment phase of detachment retinopathy which may be present for years may be subdivided as follows

(A) Initiating Sequence
(B) Degeneration hole Sequence
(C) Hole Detachment Sequence

We are of course interested in the types of patients with a certain predominance in retinal detachment whose population (being the population at risk') is low in the general population, and who are likely to be in attendance at an ophthalmic department

With these considerations in mind the following types of patients are being especially examined for the presence of pre detachment retinopathy

(1) The 'second eye in all cases of retinal detachment
(2) All cases of aphakia with myopia
(3) All cases presenting symptoms suggestive of detachment retinopathy

In most of the departments involved in this study, special clinics have been set up for the investigation of these types of patients These departments are prevention detachment minded and have photocoagulation equipment at their service

B TO PROVE THAT RETINAL DETACHMENT HAS BEEN PREVENTED

Preventive retinal detachment may be said to have been begun on an intensive scale in Israel in January 1960 The rate of incidence of retinal detachment per 100 000 of the population over 40 years of age in the four years (1956–1959) is shown in Fig 4 and will be compared with that of the ten succeeding years (1960–1969) Special reference will be made to the incidence among second eyes and aphakic myopes In addition note is made of all cases of preventive therapy carried out since 1960 and an association sought between the number of these cases and any change that may be noted in the incidence of retinal detachment during the 1961–1969 period During the 1960–69 period the following data from each department will be received

(*a*) The total number of eyes operated on for retinal detachment
(*b*) The number of second eyes in the total number of eyes operated on for retinal detachment
(*c*) The number of aphakic myopic eyes in the total number of eyes operated on for retinal detachment
(*d*) The number of preventively treated eyes
(*e*) The number of second eyes treated preventively
(*f*) The number of aphakic myopic eyes treated preventively

C TO DETERMINE THE NATURAL HISTORY OF THE PRE DETACHMENT PHASE OF RETINAL DETACHMENT

To achieve this as many as possible cases of suspected detachment retinopathy in the pre-detachment phase have completed with respect to them an investigation sheet which is common to all the departments in the country (Fig 5) In this sheet are noted data regarding history symptomatology and ophthalmoscopic changes

The problems implicit in A (initiating sequence) probably depend for their solution on histological studies, while those of *B* and *C* (degeneration hole sequence and hole detachment sequence) may well be clarified by an organised large scale clinical study which is now being described

In order to attempt to answer these questions of clinical pattern and those of proof of the efficacy of preventive measures, the 7 main ophthalmic departments in Israel have been combined in a cooperative study These departments have a total of 207 beds Quarterly statistics of preventive measures, and detachment incidence are centralised for review In addition a common case history sheet is used, the facts on which are periodically transferred to a central system of marginal punch cards Between 1956 and 1959 (preventive therapy may be considered to have begun in 1960), about 180 retinal detachment eyes were treated each year The purpose of this communique is to describe the methods used in this study and to give a preliminary report on the results achieved and expected

METHODS AND MATERIAL

A The discovery and treatment of eyes with pre detachment changes

As already stated, patients with pre detachment changes either come to the doctor with complaints of muscae or flashes, or, having little or no symptoms, must be sought out and brought to examination Concerning the latter, there are certain types of individuals that are liable to retinal detachment The following table lists the main types of patients found in retinal detachment cases, their percentage incidence as noted in published reports, their percentage incidence in cases occurring in Israel between 1956 and 1959, and the estimated number of patients of each type at risk in Israel in 1960

Types of Individuals	*Average % Incidence of types in cases of Detachment reported in World literature*	*Average % Incidence of types in cases of Detachment in Israel 1956–1959*	*Number of Cases at risk in Israel in 1960*
Myopia less than 5 D	25 %	30 %	about 95 000
Myopia 5 D or over	37 %	40 %	about 95 000
Aphakia	10 %	11 %	7 000 8 000
Myopia and Aphakia	7 %	8 %	1 000
Second Eyes'	20 %	12 %	1 000

SUR L'IMPORTANCE DE LA DEFECTOSCOPIE ULTRA SONIQUE DANS L OPHTALMOLOGIE

JAN VANYSEK ET JULIANA PREISOVÀ

De La Clinique D ophthalmologie De L universite J Ev Purkyne A Brno Chef De Clinique Prof Mudr Jan Vanysek Dr Sc

Notre travail preliminé sur l utilisation d'un examen apparemment simple de l œil humain par un defectoscope ultrasonique a impulsion introduit dans l ophtalmologie par Mundt et Hughes (1) et qui a ete elaboré depuis 1957 surtout par Oksala (2-17) a montré que cette méthode bien que certainement de valeur, n a pas une valeur univoque de preuve

L interpretation des courbes dans les echogrammes des tissus normaux et pathologiques intra-oculaires parait souvent contestable Quelques échos, désignes comme reflet surtout de corps etrangers à l intérieur de l oeil pour la plupart pas contrastants par rayons X n out jusqu à présent pas cette possibilite de preuves demandee par le clinicien à une telle méthode Cette imperfection des resultats de Oksala et aussi des notres a conduit à un scertain scepticisme que l on trouve aussi dans le travail de Baum et de Greenwood (18) Ces derniers auteurs ont en 1961 apprecié a leur juste valeur 16 travaux de Oksala et son interprétation des echogrammes pathologiques Baum et Greenwood ont çertes employe des appareils provenant d une autre usine que ceux d Oksala mais ils ont travaille avec des sondes de la meme fréquence dans des conditions a peu pres parailles Ils consideraient les resultats d Oksala comme contestables

A notre clinique nous travaillons depuis plus de deux ans avec la défectoscopie ultrasonique Nous avons déja publie nos premiers résultats (19) Les principaux devoirs que nous nous sommes poses dans notre travail étaient la mesurage de plusieurs distances dans l oeil c est à dire la mensuration de la profondeur de la chambre anterieure et de l axe optique de l oeil, puis le diagnostic par rayons X de corps etrangers non contrastants et dans les derniers temps surtout le diagnostic differenciel de decollements simples et secondaires de la rétine

METHODIQUE

Les examens ont été effectues au moyen d'un défectoscope ultrasonique de la firme Kretz 1000 M avec une sonde de barium — titanat d une frequence de 6 M Hz d un diametre applique de 6 mm. Au cours de ces examens nous avons trouve que la meilleure methode etait de travailler avec l impulsion 2 et le renforcement 10 Si nous avons employé une autre impulsion ou une sonde d une autre frequence

which may be relative to the case Information regarding any preventive measures carried out is noted Details regarding the state of the vitreous and changes *in the fundus*, including pigmentation, choroidal changes, lattice formation, cystoid degeneration and hole formation, are so arranged, that they can be transferred to marginal punch cards Periodically these *case sheets* are centralised into a central office, where any new information is transferred to the punch card record The case sheets are then returned to the various departments The information on the *punch cards will* be analysed *with* respect to the problems of the natural history of the pre detachment phase already detailed

RESULTS

Despite the 369 eyes that have been preventively treated since 1960, there is no change in the incidence of retinal detachment in the *population during the years 1960, 1961* and *1962*, the necessary corrections having been made for increase and ageing of the population This may mean either that only a small percentage of the eyes treated *would, if untreated*, have developed retinal detachment, or *that* the latency between hole discovery and detachment formation is longer than the period under observation Two out of the 5 cases with retinal *hole, which ultimately developed detachment, observed by* Colyear and Pischel (1956), did so after 1 year and 2 years and 9 months respectively It is obvious that further observation over a number of *years will be required in order to indicate the extent to which the* incidence of retinal detachment may be affected by means of preventive measures

Besides the unknown, but probably years *long latency* between hole formation and retinal detachment, there are other, chiefly organisational factors, which indicate that the expected fall in incidence will gather momentum after a few years *The retinal clinics* are *being* more organised to deal with the patient who, because of symptoms or because he falls within the group of second eyes or myopic aphakics, is a candidate for detachment, and the general ophthalmologist is becoming more aware of the possibilities of preventive therapy

If we assume a straight line from the pre test period average of 27 6 p 100,000 to half that number *(13 8 p 100,000) during 10 years* the rate should, after 5 years be at 75% of the original, at 20 7 In view of the fact that — as experience of the first years of the test period *has shown* — it will take some years *until the preventive* observation programme will be in full operation, we will assume arbitrarily that after 5 years only 85% rather than the level of 75% will be reached *This would give* us the rate of (85% of 27 7 =) 23 5 for the year 1964

The period of observation is too short to permit definitive observations regarding the evolution *of the* pre detachment *phase* of retinal detachment The method of a national cooperative study seems however, to be a valid one for answering the problems posed, and *it is hoped* that it may *be possible* to contribute to their solution in further reports

I F S 42 ans, num 174/62 Dans l anamnese il voyait un rond devant l oeil droit pendant deux mois

VOD 6/60 sl + 2 0 comb + 1 0 cyl axe 90°
6/36
VOS 6/15 + 2 0 comb + 1,5 axe cyl 120°
6/15

Sur le fond de l oeil droit il y a nasalement et temporalement de la papille un relevement spherique de la retine avec des signes caracteristiques d'une croissance de tumeur La tension intraoculaire est de 24 mm/Hg Par la lampe de Lange par voie non operative la malformation n etait pas accessible L epreuve du melanin dans l urine dans un des examens etait positive

L examen ultrasonique de l oeil droit de nombreux echos pathologiques d apres l emplacement de la sonde, prouvent les reflets d une malformation massive La localisation est conforme à l examen ophtalmologique (Fig 1) Au cours de l *examen macroscopique* du bulbe énuclee nous avons constaté un melanoblastome de la choroide à l endroit decrit c est a dire dans *le quadrant* supero-temporal pres du pole posterieur une malformation *typique* de la forme d un champignon grisâtre blanchatre d une grandeur de 7 × 8 mm (Fig 2)



FIG 1 Echogramme numero 1303 Malade F S numero d observation 174 62 Diagnostic Melanoblastome choroidea oc dx La sonde a été appliquee dans le mérid n de IV h à une distance de 3 mm du limbe

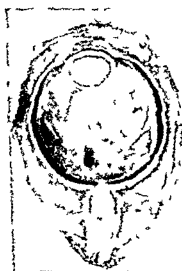


FIG 2 Le même malade Coupe longitudinale du bulbe enuclée montrant la tumeur d une grandeur de 7 × 8 mm dans le quadrant supero—temporal.

nous citons ce fait toujours au cours de l'examen meme Ce n'est que depuis deux mois que nous pouvons employer le dernier appareil Kretz 7000, approprie specialement a l'emploi medical, tandis que l'appareil precedent avait ete construit surtout pour la metallurgie En attendant il nous est impossible de comparer les resultats obtenus avec les deux appareils Mais on peut dire preliminairement que l'appareil Kretz 7000 aura beaucoup d'avantages Nous avons effectué l'anesthesie de l'oeil avec 5% de cocaine Comme moyen de liaison nous avons employe de la paraffine liquide Nous avons enregistré toutes les constatations par photographie Nous avons applique la sonde tantot dans le centre de la cornee, tantot sur le limbe dans le meridien 3, 6, 9 et 12 h et plus, sur la sclerotique a une distance de 6 8 mm du limbe dans les memes meridiens Nous avons toujours tache d'appliquer la sonde de façon a ce que l'axe des rayons ultra soniques passe du moins approximativement par le centre du bulbe Chez tous les malades nous avons aussi examiné l'autre oeil

Mise au point des resultats Jusqu'a present nous avons fait environ 1700 photographies d'echogrammes ce qui correspond a un double nombre d'examens effectues Tous les cas de caractere banal ou repetes avec le meme resultat n'ont pas ete photographies Dans notre premiere communication nous avons cite positivement les possibilites de localisation de corps etrangers dans l'oeil interieur par l'ultrason Dans ce groupe provisoire notre matériel n'est ni assez etendu, ni assez edifiant pour pouvoir des aujourd' hui essayer de donner une appreciation a sa juste valeur La localisation de corps etrangers dans l'interieur de l'oeil par la defectoscopie ultrasonique doit en attendant tre consideree comme methode moins fiable et qu'il faut encore elaborer, c'est le cas pour beaucoup d'echos sub ordonnes causes par une hemorragie, une exsudation une proliferation du tissu et par d' autres malformations pathologiques refletant l ultrason et a cause d'une assez grande zone morte de la sonde emplo yee Malgre que nous ne soyons pas sceptiques nous voulons ne pas faire d'erreurs provenant d'experiences peu etendues et insuffisantes

Dans cette communication nous voulons faire part de 3 groupes d'examens, ce sont

A Les malades du decollement de la retine cachant une tumeur intraoculaire

B Les malades avec un decollement primaire de la retine

C Les personnes examines avec defaut refractaire ou la defectoscopie ultrasonique devait determiner la longueur de l'axe optique de l'oeil

Dans le premier groupe des malades avec un decollement de la retine cachant une tumeur intraoculaire, nous avons choisi 10 malades ou apres l'enucleation de l oeil il a ete possible de confronter le diagnostic ophtalmologique et les examens auxiliaires avec les examens ultrasoniques et histologiques Nous donnons le compte rendu de ses malades en resumé

3 A J , 55 ans, numero 1269/62

Dans l anamnese perception visuelle abolie de l oeil gauche pendant pres de deux mois Suspecte d un decollement primaire elle a ete soignee dans un autre hopital et seulement trois semaines apres elle a ete envoyee à notre clinique

VOD mouvement, projection juste

VOS 6/8 + 0,5 D 6/6

Sur la retine de l oeil droit il y avait deux decollements spheriques sans dechirures dont l un couvrait la moitie nasale entière le deuxieme le quadrant infero temporal Le melanin dans l urine etait faiblement positif par l examen avec la lampe de Lange nous avons constate dans la moitie nasale un assombrissement important L examen ultrasonique a donne deux sortes de constatations Dans plusieurs projections nous avons constate isolement un echo pathologique correspondant au sommet de la retine decollee

En appliquant la onde a XI h a 10 mm du limbe nous avons vers la fin de l echogramme eu de nombreux echos pathologiques temoignant pour une malformation solide Apres l enucleation du bulbe nous avons constate un melanoblastome spinocellulaire localise sous la region centrale d une grandeur de 12 × 6 mm

4 A S 59 ans numero 1278/62

Dans l anamnèse vision d un fil devant l oeil droit pendant 5 mois

VOD 4 m doigts

VOS 6/12

À l oeil droit nous avons constate un decollement de la retine de V a VII h qui avait toutes les marques d un decollement primaire sans dechirure De XII a IX h il y avait un decollement gris de caractère plutot sphérique se terminant abruptement L examen avec la lampe de Lange montre un assombrissement vers VII h L epreuve du melanin dans l urine etait négative La tension intraoculaire etait de 24 mm Hg L examen ultrasonique a montre un type d echogrammes demontrant un simple decollement et un autre type demontrant par de nombreux echos une tumeur selon l application de la sonde L application de la sonde etait particulierement demonstrative contre l endroit de la tumeur suspecte (Fig 5), et au dessus de la tumeur (Fig 6) ou les echos typiques etaient soit a la fin soit au commencement de l échogramme Apres l enucleation nous avons constaté dans le quadrant infero — temporal de l oeil droit immediatement derrière l equateur un melanoblastome de la forme d un champignon d une grandeur de 6 × 7 mm (Fig 7)

5 V J 60 ans numero 1222/62

Dans l anamnèse le malade a signale que trois jours avant sa venue à l hopital il a senti de grandes douleurs a l oeil gauche et qu il a

2 C J, 46 ans, numero 262/62 Dans l'anamnese il y a 4 mois blesse a l'oeil gauche d'une contusion par une pierre À present il voit mal de cet oeil depuis 2 mois Dans un autre hopital il a été soigne conservativement d'un decollement primaire de la rétine Après insucces de la therapie il a ete envoye a notre clinique pour etre examine

VOD 5/5
VOS 1 m doigts

À l'oeil gauche, decollement gris de la retine abruptement limité vers la papille, plus plat vers la periphérie Sur le decollement pigmentation isole La lampe de Lange brille partout, tension intra oculaire 15 mm/Hg

Examen ultrasonique l'application de la sonde, a IX h sur le limbe a montre de nombreux echos pathologiques, temoignant du



Fig 3 *Echogramme numéro 1329* Malade C J numero d observation 262/62 Diagnostic Melanoblastome chorioideae oc sin La sonde a eté appliquée dans le méridien de IX h à une distance de 5 mm derrière le limbe



Fig 4 Le meme malade Coupe longitudinale du bulbe enucléé montrant la tumeur d une grandeur de 6 × 11 mm dans le moitié temporale du bulbe atteignant la région centrale

reflet d'une matiere massive devant la *fin du bulbe* (Fig 3) Apres l enucleation, apres l ouverture du bulbe fixe, nous avons constate un *melanoblastome* dans la region centrale de l oeil gauche, surtout dans la moitie temporale, d une grandeur de 6 × 11 mm, la retine au dessus etait decollee (Fig 4)

3 A J 55 ans numero 1269/62

Dans l anamnese perception visuelle abolie de l oeil gauche pendant près de deux mois Suspecte d un décollement primaire elle a ete soignee dans un autre hopital et seulement trois semaines apres, elle a ete envoyee a notre clinique

VOD mouvement, projection juste

VOS 6/8 + 0 5 D 6/6

Sur la retine de l oeil droit il y avait deux decollements spheriques sans dechirures dont l un couvrait la moitie nasale entiere le deuxieme le quadrant infero temporal Le melanin dans l urine etait faiblement positif, par l examen avec la lampe de Lange nous avons constate dans la moitie nasale un assombrissement important L examen ultrasonique a donne deux sortes de constatations Dans plusieurs projections nous avons constate isolement un écho pathologique correspondant au sommet de la rétine décollee

En appliquant la sonde à XI h, à 10 mm du limbe nous avons vers la fin de l échogramme eu de nombreux echos pathologiques temoignant pour une malformation solide Apres l enucleation du bulbe nous avons constate un melanoblastome spinocellulaire, localise sous la region centrale d une grandeur de 12 × 6 mm

4 A S, 59 ans numero 1278/62

Dans l anamnese vision d un fil devant l oeil droit pendant 5 mois

VOD 4 m doigts

VOS 6/12

À l oeil droit nous avons constate un décollement de la retine de V à VII h qui avait toutes les marques d un decollement primaire sans dechirure De VII à IX h il y avait un décollement gris de caractere plutot spherique se terminant abruptement L examen avec la lampe de Lange montre un assombrissement vers VII h L epreuve du mélanin dans l urine était negative La tension intraoculaire etait de 24 mm Hg L examen ultrasonique a montre un type d echogrammes demontrant un simple decollement et un autre type demontrant par de nombreux échos une tumeur selon l application de la sonde L application de la sonde était particulierement demonstrative contre l endroit de la tumeur suspecte (Fig 5), et au dessus de la tumeur (Fig 6) ou les echos typiques etaient soit à la fin soit au commencement de l échogramme Apres l enucléation nous avons constaté dans le quadrant infero — temporal de l oeil droit immediatement derrière l equateur un melanoblastome de la forme d un champignon d une grandeur de 6 × 7 mm (Fig 7)

5 V J 60 ans numéro 1222/62

Dans l anamnese le malade a signalé que trois jours avant sa venue à l hopital il a senti de grandes douleurs à l oeil gauche et qu il a



FIG 5 *Echogramme numero 1583* La malade A S numéro d observation 1278/62 Diagnostic Melanoblastome chorioideae oc dx La sonde a été appliquée dans le meridien de II h à une distance de 6 mm du limbe directement *contre* la tumeur

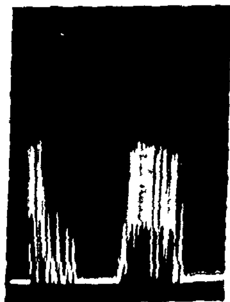


FIG 6 Echogramme numero 1587 La meme malade La sonde a ete appli quee audessus de la tumeur dans le méridien de VII h à une distance de 10 mm du limbe



FIG 7 *La meme malade* Coupe longitudinale du bulbe enuclee *montrant la tumeur* dans le quadrant inferotemporal d une grandeur de 6 × 7 mm

tout d un coup cessé de voir Apres 2 jours dans un autre hopital il a ete envoye à notre clinique

VOD 6/6

VOS 0

À l oeil gauche les deux paupieres et aussi la peau du cote gauche de la joue était oedemateuse la mobilite du bulbe vers le bas et vers la tempe etait limitee La conjonctive bulbaire chemotique dans la moitie inferieure du bulbe prolabait au dehors entre les paupieres La cornee etait grisatre, de surface finement bosselee hyperhemie de l iris Le réflexe rouge etait inexistant Le bulbe en protrusion de deux mm Après une therapie conservative anti inflammatoire et contre glaucomateuse il a ete possible de voir un profond decollement spherique de la retine gris vert de V a X h couvrant la papille La tension intraoculaire etait de 62 a 42 mm/Hg L examen avec la lampe de Lange a montre un assombrissement entre IV a VI h examen ultrasonique a montre a l application de la sonde sur le limbe a IX h plusieurs echos pathologiques places etroitement l un a cote de l autre comme reflets d une malformation massive Apres l énucléation nous avons constate vers le pole posterieur une tumeur plate d une hauteur de 5 mm d une longueur de 17 mm

6 J K 63 ans numero 1270/62

Dans l anamnese elle a observe durant les deux derniers mois une perception visuelle amoindrie de l oeil droit

VOD 2 mètres et demi doigts

VOS 6/10 sl

À l oeil droit la retine etait decollee dans le quadrant infero nasal et dans toute la moitie temporale Entre IX et I h, elle était à la peripherie gris foncé autre part grisclair la tension intraoculaire etait de 25 mm/Hg L examen avec la lampe de Lange demontrait un faible assombrissement entre X et I h a une distance de 10 mm du limbe l examen ultrasonique a demontré des echos pathologiques presque dans tous les méridiens Du cote nasal nous avons constate un type d échos temoignant d un simple *décollement* de la retine dans le quadrant infero temporal et un type de nombreux echos temoignant d une malformation massive *devant* la paroi posterieure du bulbe à l application de la sonde contre la tumeur suspecte (Fig 8)

Après l enucléation du bulbe nous avons constate un melanoblastome s étendant depuis la racine de l iris jusqu au pole posterieur presque sur toute la moitie postérieure du bulbe plutot vers le quadrant supéro-temporal Il etait plat d une hauteur de 4 à 5 mm (Fig 9)

7 F J 77 ans numéro 416 62

Dans l anamnèse elle a ete traitee depuis sa soixantième annee d une anemie pernicieuse

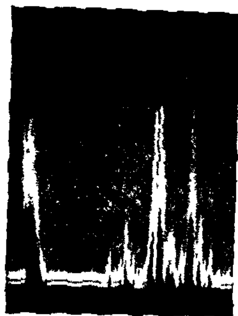


Fig 8 Echogramme numero 1559 La malade J K numero d observation 1270/62 Diagnostic Melanoblastoma choroideae oc dx La sonde a ete appliquee contre la tumeur dans le meridien de II h sur le limbe



Fig 9 La meme malade Coupe longitudinale du bulbe enucléé montrant la tumeur d une hauteur de 4 mm remplissant presque toute la moitie posterieure du bulbe

Une semaine auparavant la malade a ressenti des douleurs à l oeil droit et celui ci etait rougi

VOD projection lumineuse defective

VOS 6/15 sl + 2,00 D 6/6 sl

La peau de la paupiere inferieure et de la moitie superieure de la joue droite etait rougie, tout la conjonctive bulbaire etait chemotique Sur le fond, un decollement haut de la retine avec trois ballons de II a V h, de V a VIII h et de VIII a XI h,

L'examen avec la lampe de Lange la pupille ne brillait pas de XII a X h

La tension intraoculaire etait de 15 mm/Hg

L'examen ultrasonique a demontre des echos typiques, nombreux, place tres densement l'un a cote de l'autre, pas tres hauts et cela surtout sur l'echogramme entier a l'application de la sonde a IX h (Fig 10) Apres l'enucleation on a trouve dans le corps ciliaire et dans la choroide, dans le quadrant infero temporal, un melanoblastome de 14 × 9 mm, la retine devant lui etait decollee (Fig 11)

8 M D, 58 ans, numero 1042/62

Dans l'anamese perception visuelle amoindrie de l oeil droit pendant 4 mois Pendant ce temps la malade a ete traitee dans l ambu



FIG 10 Echogramme numéro 1367 La malade F J numéro d observation 416 62 Diagnostic Melanoblastoma corporis ciliaris et chorioideae oc dx La sonde a été appliquée dans le méridien d IX h à 3 mm derrière le limbe au dessus de la tumeur

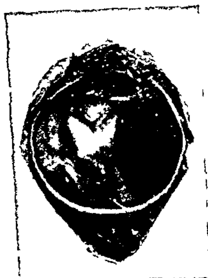


FIG 11 La même malade Coupe longitudinale du bulbe enuclée montrant la tumeur dans le quadrant inferotemporal d une grandeur de 14 × 9 mm

lance par le medicin du secteur, d une tension intraoculaire augmentée bilatérale 4 jours auparavant la malade a eu une attaque glauco mateuse de l oeil droit

VOD projection de lumière seulement temporale

VOS 6 24 + 1 5 D 6 6

Les deux paupieres de l oeil droit étaient enormement enflees la conjonctive bulbaire etait chemotique La cornee grisatre finement bosselée l iris congestionnee La lentille etait diffusement troublee A l examen avec la lampe de Lange nous avons constaté que dans la moitié temporale la pupille ne brillait pas La tension intraoculaire originale 49 mm Hg a eté normalisée par un traitement conservatif a 15 mm Hg L examen ultrasonique a demontre de nombreux echos pathologiques typiques pas trop hauts et places très pres l un de l autre echos d une malformation massive et cela a l application de la sonde d une part contre la moitié temporale du bulbe dans les deux tiers de l echogramme posterieur (Fig 12) et au commencement de l echogramme à l application de la sonde dans la moitie temporale du bulbe (Fig 13) Après l enucleation nous avons constate un melanoblastome remplissant le quadrant supero temporal d une grandeur de 16 × 10 mm (Fig 14)

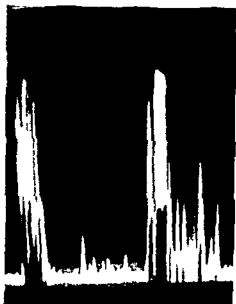


FIG 12 Echogramme numero 1492 La malade M D numéro d observation 1042/62 Diagnostic Melanoblastoma chorioideae oc dx La sonde a été appliquée dans le méridien de III h au dessus du limbe contre la tumeur



FIG 13 La meme malade Echogramme numero 1498 La sonde a ete appliquee *dans le meridien* de XI 1/2 h au dessus de la tumeur

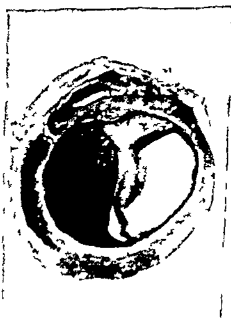


FIG 14 La meme malade Coupe longitudinale du bulbe énuclee montrant *la tumeur dans* le quadrant supero temporal d une *grandeur de* 16 × 10 mm

9 F N , 58 ans numero 1016/62

Dans l anamnèse perception visuelle amoindrie de l oeil droit durant quatorze jours

VOD 2 metres et demi doigts

VOS 6/8 + 0,75 D 6/6

Sur le fond de l oeil il y avait un décollement spherique de la retine s etendant jusqu à la papille de IV a VIII h , sans dechirure L examen avec la lampe de Lange a montre le meme rayonnement amoindri entre la VI et la VII La tension intra oculaire etait de 15 mm/Hg

L examen ultrasonique n a pas reussi a demontrer des echos qui aurait fait suspecter une malformation massive, mais seulement des echos pathologiques d une retine decollee Apres un certain tempt d observation nous avons pourtant enucleé le bulbe etant suspect d une malformation tumereuse Apres l enucleation nous n avons pas vu de marques d une tumeur du bulbe droit Dans le sang nous avons constaté par electrophorese sur le papier une gamaparaproteinemie

10 B M 74 ans numéro 1330/62

Dans l anamnese perception visuelle limitee de l oeil droit pendant 4 mois

VOD 1/2 m doigts exc

VOS 6/15 + 16/10

La retine de l oeil droit decollée de IV a VIII h jusqu a la papille La surface de la retine grisatre brunatre avec des hemorragies isolées La tension intra oculaire était de 15 mm/Hg L examen avec la lampe de Lange a montré un assombrissement total de la pupille de V a VIII h L examen ultrasonique a demontre des echos pathologiques d une malformation massive au commencement de l echogramme à l application de la sonde dans le quadrant infero temporal À l application de la sonde dans le quadrant supero nasal il y avait de nombreux échos places a la fin de l echogramme et fondus à l echo final du bulbe Par l examen histologique nous avons constate qu il s agissait d un mélanoblastome de la choroide d une grandeur de 14 × 5 mm dans le quadrant infero-temporal

Par contraste à ce groupe de malades que nous avons du point de vue clinique considerés comme suspects d une croissance de tumeur intra-oculaire il y a un groupe de malades ou tous les examens cliniques ont temoigne pour un simple decollement retinien

1 J O 61 ans num 471/62 Dans l anamnese il a eu une perception visuelle amoindrie de l oeil droit pendant 1 jour

VOD 2 m kor nel

VOS 2 m — 20 O D 6/36

À l'oeil droit decollement spherique de la retine dans la moitié superieure avec une dechirure en fer a cheval dans la peripherie

À 12 h la lampe de Lange brille partout La tension intra oculaire normale L'examen ultrasonique a montre un echo hautement pathologique de la retine decollee au cours de application de la sonde dans la direction opposee du decollement

2 F M, 65 ans, num 1178/62 Dans l'anamnèse elle avait l'impression d'une mouche qui se posait devant l oeil droit, durant 4 mois, et au cours du dernier mois elle se plaignait d'une perception visuelle amoindrie

VOD mouvement, projection correcte

VOS 5/5

La retine de l'oeil droit est decollee dans toute l'etendue de la moitie temporale jusqu'a la papille La lampe de Lange brille partout La tension intra oculaire 15mm Hg Sans constatation de dechirure L'examen ultrasonique a montre un écho hautement pathologique, revenant completement a la base temporel au cours de l'application de la sonde contre le decollement

3 M G, 65 ans, num 1268/62 Dans l'anamnese epistaxis recidivante, trombose de la veine centrale de l'oeil gauche deux ans auparavant et une vision diminuant rapidement 4 mois auparavant

VOD 5/7,5

VOS amaurosis

À l'oeil gauche dans le corps vitre un nombre de petites opacites La retine est decollee dans toute son etendue La tension intra oculaire est 12 mm/Hg La lampe de Lange brille dans tous les sens L'examen ultrasonique a montre a l'application de la sonde presque dans tous les meridiens un echo hautement pathologique, dans l endroit correspondant au sommet de la retine decollee

4 M V 52 ans, num 1301/62 Dans l'anamnère il a observe pendant 3 mois qu'il ne voyait pas, en lisant, la partie superieure des lettres

VOD 5/15 + 1,00 5/15

VOS 5/50 + 2,00 + 2,00 c/t ax 90° 5/24

À l'oeil gauche la retine est decollee depuis 3 a 8 h jusqu'à la papille platement

L'examen ultrasonique a montre l echo bas isole pathologique dans l'endroit du sommet seulement d un decollement plane de la retine

5 J K 67 ans num 1292/62 Dans l anamnese il a observe pendant 6 semaines une ombre devant l oeil droit Apres un traitement conservatif dans un autre hopital il a ete envoye chez nous

VOD 1 m
VOS 5/5 *sl*

A l oeil droit la retine est decollee dans toute l'etendue de la moitie temporale L examen ultrasonique a montre a l application de la sonde contre le decollement de la retine 1 haut echo pathologique dans l endroit correspondant

Le dix neuvieme jour apres une operation reussie du decollement *nous avons* de nouveau effectue un examen ultrasonique qui a montre un echogramme tout a fait normal sans echo pathologique

6 F Z 57 ans num 602/62

Dans l anamnèse une grave myopie bilaterale depuis la jeunesse et une semaine auparavant vision de fils et de taches noires devant l oeil gauche

VOD 3/4 m doigts
VOS 2 m exentriquement

A l oeil gauche la retine est decollee dans toute l *etendue de* la moitie temporale jusqu a la papille 2 dechirures dans le *meridien* 1 et 2 h L examen ultrasonique a *montre* a l *application de* la sonde a 5 mm du limbe à 7 h un echo pathologique

7 F H 51 ans num 479/62

Dans l anamnese le malade avait été blesse il y a 2 ans 2 fois par contusion a l oeil *droit Depuis* ce temps la perception visuelle de l oeil droit diminuait *graduellement*

VOD mouvement projection du cote nasal defective
VOS 6/6

A l oeil droit il y a dans le corps *vitré de nombreuses* hemorragies la retine est decollée dans toute son etendue L examen ultrasonique a montre un écho pathologique de *hauteur* moyenne a l application de la sonde contre la retine decollee

8 J S 54 ans num 121/62

Dans l anamnèse après l extraction d un corps etranger *et* l expulsion des masses *cristalliniennes* de la lentille il y a eu cinq mois après l accident un decollement

VOD 6/6
VOS mouvement projection *correcte*

Sur le fond de l oeil droit *autant qu il* est possible de la voir a cause d une cataracte secondaire la rétine est *décollee* dans toute son

etendue L'examen ultrasonique a montre un echo *pathologique* d une hauteur moyenne dans l'endroit du decollement en employant une sonde de $10MH_z$ a *impulsion* 1

9 J P 23 ans, *num* 285/62 Dans l'anamnese le jour de sa venue par hazard constatation d'une maladie de l'oeil gauche

VOD 6/6

VOS 1 metre et quart doigts

La retine de l'oeil gauche est decollee dans toute l'etendue de la moitie temporale et dans le *quadrant nasal inferieur* Le decollement de la retine de l'ora serrata entre 4 et 5 h L'examen ultrasonique a montre un echo de hauteur moyenne dans l'endroit du sommet de la retine decollee

10 V B, 37 ans, num 1898/62

Dans l'anamnese une grave myopie bilaterale depuis la jeunesse et pendant les trois derniers jours une perception visuelle diminuee de l'oeil droit

VOD sensibilite a la lumiere projection correcte

VOS 2,5 m doigts — 16 D 6/36

La retine de l'oeil droit est décollee dans presque toute son *etendue, il ne reste qu'une mince bande nasale ou elle est adherente* L'examen ultrasonique a montre a l'application de la sonde contre de la retine decollee des echos pathologiques sporadiques dans toutes les directions

Si nous apprécions ces deux groupes à leur juste valeur nous pouvons dire que la croissance de tumeurs, soit visible, ou cachee, a *toujours* au cours de l'examen ultrasonique donne un échogramme carasteristique, compose d'un nombre d'echos pathologiques, entre la retine decollee au dessus de la tumeur et la fin du bulbe pratiquement determine par la paroi sclerotique

Ces echos pathologiques rappellent par leur arrangement les oscillogrammes obtenus dans la defectoscopie technique pour mesurer par exemple la grosseur de la tole et ils sont proprement dit une suite d'impulsions multiples

Au contraire, ces echos nombreux n'ont jamais ete constates en cas d'un simple decollement de la retine Nous supposons que le tissu massif de la tumeur a par sa composition donne les conditions necessaires a de nombreux *echos d ondes ultrasoniques*, tandis que le decollement simple donnait *la* possibilite d un echo par *la retine* decollee et seulement apres, par le tissu du reste adherent *de la retine de la choroide* et de la sclerotique Nous avons pris pour tumeur dans le premier groupe aussi un cas d un simple decollement de la retine chez se malade *nous avons constate en meme* temps une paraproteinemie, et, par mefiance de l'echogramme qui temoignait pour un simple decollement, nous avons effectue *l énucleation du bulbe*

(malade decrit dans le premier groupe sous le numero 9) Nous voudrions attirer l attention sur une constatation typique la tumeur decrite dans le premier groupe comme numero 8 ou une serie d echos pathologiques apparaissant l un apres l autre a ete constatee soit au commencement de l échogramme ou à la fin de l echogramme selon que la sonde a ete placee contre la sclerotique au dessus de la tumeur ou dans la situation opposee A cause de la conformite des enregistrements photographiques de ces malades a un simple decollement nous en citons seulement deux cas typiques qui ne diffèrent toutefois guere des autres Enregistrement au cas decrit sous le numero 5 (Fig 15)

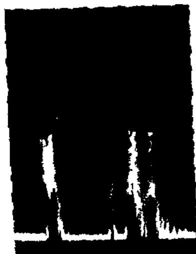


FIG 15 Echogramme numero 1596 Le malade J K numéro d observation 1292/62 Diagnostic Amotio retinae idiopatica oc dx La sonde a ete appliquee dans le meridien de III h près du limbe

Par les *résultats obtenus des deux groupes* je suppose qu il est possible de distinguer avec surete par la defectoscopie ultrasonique le *decollement secondaire* qui recele une tumeur du décollement primaire de la *ret ne si* la condition est remplie que la tumeur se trouve dans l axe *des rayons emis par la* sonde Theoriquement il serait possible de *prendre* d apres *l* echogramme pathologique une tumeur pour un neoplasme avec decollement qui recèle une exsudation organisee (pseudotumeur)

Dans les derniers temps nous avons tache d employer la defectoscopie ultrasonique *pour la mensuration* de la longueur de l oeil

Avec cette methode il est *possible* de mesurer la distance entre l endroit de l attouchement de la *sonde* d oeil c est a-dire entre l epithelium de la cornee et le *premier tissu dans la* partie posterieure de l oeil donnant un echo, c *est a-dire la* retine Du point de vue technique on peut bien lire *sur l echogramme* l echo de l entree et le premier d un nombre d echos de la paroi postérieure du bulbe qui correspond à la retine *Pour effectuer* cette mensuration il faut que la

distance de deux marques dans la ligne basale de l'image soit 20 mm dans l'eau Nos mensurations repetees avec nos emetropes sous ses conditions ont determine la longueur de la distance entire la cornee et la retine a 1,8 cm

Toutefois ce resultat etait en contradiction avec les mensurations du bulbe pratiquees jusqu'a *présent* *Tabulae biologicae citent* que l'axe sagitale de l'oeil est d'une longueur de 24 mm Si nous soustrayons *de cette longueur de l'oeil*, l'epaisseur de la sclérotique 1,3 mm, l'epaisseur de la choroide 0 3 mm et l'epaisseur de la retine 0 3 mm, cela fait en tout 1,9 mm, Nous devrions donc obtenir une longueur de 24 mm — 0,9 mm, c'est a dire une longueur moyenne de 22,1 mm, qui represente la distance entre l'epithelium de la cornee et la surface de la retine Notre resultat qui differe a peu près de 1 mm est explicable par la vitesse d'une grandeur inegale de la propagation des ondes ultrasoniques dans la cornee, dans l humeur aqueuse, dans le cristallin et dans le corps vitre, qui differe de la vitesse de la propagation dans l'eau D apres la vitesse de la *propagation des ondes ultrasoniques* donnee par le milieu, les ondes ultra soniques penetrent par la cornee dans *0,516 µsec (= 0,8 mm/1,550 mm µsec)*

Les ondes ultrasoniques penetrent par la lentille avec 2,422 µsec (= 4 mm/1,650 mm µsec) et par l'humeur aqueuse de la chambre anterieure et par le corps vitre avec 11,47 µsec (=17,2 mm/1,495 µsec) Le total des temps ainsi calcules fait 14,408 µsec pour la dis tance de l'epithelium de la cornee jusqu'a la retine, ce qui correspond a une distance veritable de 21,55 mm

Dans ces citations sur la grandeur inegale de la vitesse de propa gation des ondes ultrasoniques par les differents tissus de l'oeil, nous expliquons la cause de la difference de la mensuration effectuee avec un appareil calibre pour une vitesse toujours egale de la propagation de l'ultra son dans l'eau Dans la pratique clinique de la mensuration nous pouvons deduire de ces conclusions mathematiques la nécessite de corriger tous les resultats obtenus jusqu'a present d environ 1 mm avec une erreur admissible, que nous n'osons pas determiner sans examens statistiques etendus, mais que dans cette etape, nous croyons etre peu importante

Apres ces mensurations nous avons essaye de mesurer des bulbes ametropiques pour acquerir *les experiences necessaires pour savoir* si cette methode peut servir a un usage pratique Nos resultats provi soires proviennent d'un nombre *relativement petit de bulbes mesures*, meme si les differentes mensurations ont ete repetees plusieurs fois pour les controler

Nous presentons la revue de ces mensurations dans le tableau numero 1

La difference des resultats montre, dans cette etape du travail que la defectoscopie ultrasonique est capable de resoudre, apres elaboration ulterieure, la mensuration *de la longueur optique* de l'oeil in situ Il faut que le probleme de la mensuration du bulbe soit

TABLEAU I — *Mensuration de la longueur de l'oeil par l'ultrason*

Numéro	*oeil*	*degré d'amétropie*	*déduction d'après l'échogramme*	*longueur corrigée de 4 mm*
1	gauche	— 14	2 3 cm	2 7 cm
2	droit	— 8	2 13 cm	2 53 cm
3	droit	— 13	2 28 cm	2 68 cm
4	gauche	— 7	2 12 cm	2 52 cm
5	droit	— 20	2 62 cm	3 02 cm
6	gauche	— 17	2 46 cm	2 82 cm
7	droit	— 16	2 56 cm	2 96 cm
8	gauche	— 7	2 12 cm	2 52 cm
9	droit	— 16	2 44 cm	2 94 cm
10	gauche	— 14	2,27 cm	2 67 cm

elaboré et que les résultats acquis avec la défectoscopie ultrasonique soient vérifiés par d'autres methodes C'est la que je vois la tache ultérieure de ce travail

Conclusion Les auteurs decrivent leurs experiences dans la differenciation entre le simple decollement de la retine et le decollement recelant une tumeur Ils supposent que d'apres les resultats actuels les nombreux echos pathologiques typiques sont un signe sur de la croissance d'une tumeur solide intra-oculaire de meme que l'echo pathologique isole est la marque d'un decollement simple, sous lequel se trouve seulement le liquide homogène sous rétinal Les résultats actuels montrent que par la défectoscopie ultrasonique on peut mesurer avec précision la longueur de l'axe optique de l'oeil in situ

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20 Tabulae Biologicae — Oculus 1947 'Pars I" Uitgeverij Dr Junk Amsterdam

THE PURPOSE OF CALIBRATION BY DYNAMOMETRY

E WEIGELIN (BONN GERMANY), A JOBSTEIN (STRASBOURG FRANCE) and P NIESEL

(Bern Switzerland)

Ophthalmodynamometry is today a valuable method for clinical investigations The results are very clear when the investigation is performed on cases with stenosis and a blockage of *one* carotid artery, as then the extremely diminished values of the affected side can be discovered Usually it is sufficient to find out whether the pulsating collapse of the central artery on the papilla takes place when the eye is subject to stress in varying degrees from the dynamometer A difference of 20% is usually significant.

This is a simple test by which a blocked carotid can be diagnosed from the positive result, if the anatomical structure of both eyes is similar and if the central retinal artery is not blocked The negative or doubtful result of the test is insignificant in about a half of our cases with blockage of the carotid or stenosis the readings were about the same in both eyes

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Difficulties in diagnosing a carotid thrombosis with the ophthalmodynamometer arise when (Fig 1)

(1) the disease is bilateral

(2) glaucoma is present with varying tension

(3) a high grade anisometropia is present

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last years, some conditions are easy to recognise, for instance anisometropia, others like glaucoma and bilateral carotid stenosis prevent us from making our investigations successful Because the test is not sufficient in these cases, we must take an additional measurement

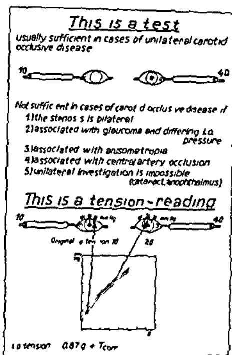


Fig 1

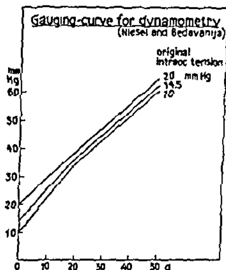


Fig 2

If we take into consideration the original tension in the eye, we can find out the diastolic and systolic blood pressure in the ophthalmic artery with dynamometry Seidel, Duke Elder and Friedenwald discovered this long time ago To measure the blood pressure, a unit must be used with which pressure in a fluid system can be measured In Biology this unit is usually mm Hg

To find out how high the tension is, when the eye is subject to a particular stress (in g), it must be measured with the applanation tonometer (DRAEGER), while the eye is subject to that amount of stress More simple still, a graph can be plotted We have done this in Bonn and Strasbourg with modern manometric methods on living and dead eyes and using the applanation tonometer The results from different methods are the same the values obtained are about the same as those which we could expect from our knowledge of the physiology of the blood circulation These values are also proved by manometric parallel measurements in the internal carotid artery Here is the graph used by us (Fig 2) and which was originally produced by Niesel and Bedavanija from applanation tonometry Today we can measure a true blood pressure of the ophthalmic artery by using the eye as a manometer

Of course it is easier to measure the blood pressure on the upper arm But then it can only be estimated whether the pressure is high,

low or normal If we measure the blood pressure in two different places we can produce more exact information We must first know the relative values of the two pressures They are very close The correlative coefficient amounts to about 0 9 for the diastolic values (Fig 3) BJÖRK found the same If one uses the middle pressure obtained from the diastolic and systolic value on both places of measurement like WEZLER and BÖGER, then the correlation becomes still higher It now amounts to 0 94 or 0 955 if the original tension in the eye is taken into consideration This means that these values are 91% dependent on each other Even if our gauging today is not always so accurate a method for investigation can easily be constructed from this basis if

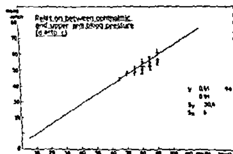


Fig 3

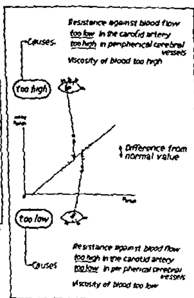


Fig 4

(1) there are pathological cases which are scattered outside the normal variations

(2) the causes leading up to pathological values are known

(Fig 4) In our book which has also now been published in English, the physical fundamentals of the method have been described in detail I would like to say here quite shortly that the pressure in the ophthalmic artery is too low in relation to the upper arm pressure when

(1) there is a raised resistance in the carotid artery usually on account of stenosis and occlusion When these are unilateral then as previously mentioned the values of the two sides are different

(2) there is a decrease of the peripheral resistance in the brain vessels This is often present with vasomotor headaches

Conversely the pressure in the ophthalmic is relatively higher than that in the upper arm when

(1) resistance in the carotid artery is decreased on account of dilatation

(2) resistance in the peripheral intracranial vessels is increased This is found in cases with the constricted type of vasomotor headaches and with most types of hypertension From the relative values of the two pressure measurements and a further formula which makes possible the differentiation between distal and proximal circulatory disorders, we can diagnose bilateral carotid thrombosis, carotid stenosis in a monocular patient when the remaining eye is on the affected side, and the already *quoted combinations In addition, it is possible to* recognise peripheral intracranial circulatory disorders The application of dynamometry has therefore very wide possibilities

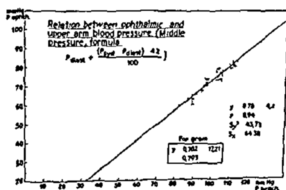


Fig 5

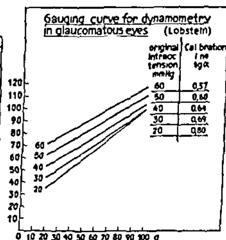


Fig 6

You will want to know whether the same results can be achieved without converting the g values which can be read directly from the dynamometer into the mm Hg values The answer is no The correlation between the g values of the dynamometer and the upper arm pressure, without considering the tension in the eye, is less exact and much lower ($P < 0{,}01$) than the relative ophthalmic pressure The mutual influence amounts to only 61% in this case against 91% The separation of the normal from the pathological cases is therefore much more difficult (Fig 5) This is because the graph is not linear — (Fig 1) It is only linear during its middle course At the beginning it rises steeply and in its higher region, *which has not yet been accurately* plotted, it is flatter Raised tension in the eye before it is subjected to the stress from the dynamometer, greatly influences the gradient of the graph (Fig 6) *This is very important if* dynamometry is used for

glaucoma research When the eye is subject to a 30 g stress taken from differing tensions the results differ considerably for the ophthalmic pressure if for instance the diastolic criterion is released

This simple dynamometric test is very useful in recognising unilateral stenosis and occlusion of the carotid When performed as a more complex examination to measure the blood pressure dynamometry could become still more useful for research in circulatory disorders and probably also in glaucoma As the subject has been dealt with on a mathematical basis it is much easier to carry out the investigation and to estimate the results as all necessary data is at our disposal on a few charts

Unfortunately it is not possible to describe here the stages of the investigation in detail

(2) there is a decrease of the peripheral resistance in the brain vessels *This is often present with vasomotor headaches*

Conversely the pressure in the ophthalmic is relatively higher than that in the upper arm when

(1) resistance in the carotid artery is decreased on account of dilatation

(2) resistance in the peripheral intracranial vessels is increased This is found in cases with the constricted type of vasomotor headaches and with most types of hypertension From the relative values of the two pressure measurements and a further formula which makes possible the differentiation between distal and proximal circulatory disorders, we can diagnose *bilateral carotid thrombosis, carotid stenosis in a monocular* patient when the remaining eye is on the affected side, and the already quoted combinations In addition, it is possible to recognise peripheral intracranial circulatory disorders The application of dynamometry has therefore very wide possibilities

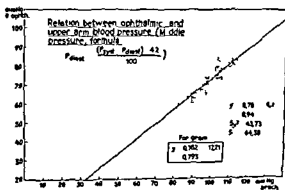


Fig 5

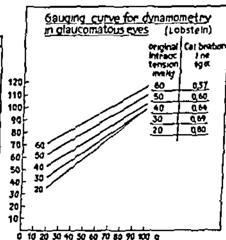


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TABLE I — *Tumours of the Orbit*

(A) Primary tumours		(B) Secondary tumours		(C) Metastatic tumours		(D) Orbital Manifestations of generalised disease	
(i) Mixed tumours of the lac gland	16	(a) Globe		(a) Ad Gland or para gan Sympathicoblastoma	3	(i) Lymphatic leucaemia	3
(ii) Dermoid cyst	15	Retino-blastoma	38	(b) Lung — Carcinoma	1	(ii) Chloroma	2
(iii) Haemangioma	14	(b) Lids — Epithelioma	2	Total	4	(iii) Hand Schuller Christian disease	1
(iv) Lymphoma	14	(c) Antrum — Sq cell carcinoma	1			Total	6
(v) Lymphosarcoma	10	Total	41				
(vi) Schwannoma	8						
(vii) Undifferenciated Sarcoma	6						
(viii) Leucaemia	6						
(ix) Glioma	5						
(x) Neurofibroma	5						
(xi) Lipoma	5						
(xii) Meningioma	3						
(xiii) Rhabdomyosarcoma	3						
(xiv) Fibroma	2						
(xv) Angiosarcoma	2						
Total	114						

TUMOURS OF THE EYE*

S P DAS,

Institute of Ophthalmology, Medical College Hospitals,

Calcutta (*India*)

650 cases of tumours of the eye were examined histopathologically in the pathology department of the Institute of Ophthalmology, Calcutta over a period of 12 years (1950-1961) All these tumours were divided into 5 groups according to their sites

I Tumours of the Orbit
II Intraocular tumours
III Tumours of the lids
IV Epibulbar tumours
V Tumours of the lacrimal passages

I Tumours of the Orbit —

The common tumours of the orbit from the present series of 165 cases are indicated in table 1 on page 1375

1 Secondary retinoblastoma
2 Mixed tumours of the lacrimal gland
3 Dermoid cyst
4 Haemangioma
5 Lymphoma
6 Lymphosarcoma

Retinoblastoma will be dealt with the connection of intraocular tumours

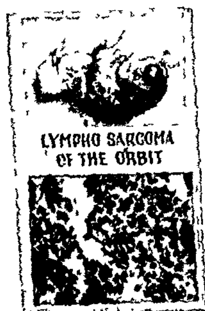
MIXED TUMOURS OF THE LACRIMAL GLAND

In the present series of sixteen cases of mixed tumours of the lacrimal gland, ten were histologically benign and six were malignant Three benign tumours later on turned into malignant and two of them died, and the other one is symptom free now So histological diagnosis of the benignity of mixed tumours of the lacrimal gland is no sure guide to the prognosis of the patient Four malignant cases died due to intracranial extension and the rest are symptom free now after radical surgery and postoperative deep X ray therapy

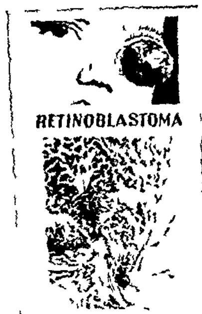
* Read at the XIX International Congress of Ophthalmology held in New Delhi 1962

HAEMANGIOMA

Twelve of the fourteen cases of haemangioma of the orbit were of cavernous variety. Surgical removal and irradiation were the two methods of treatment adopted. Observing the complications of irradiation in two cases surgical removal was employed in twelve cases and the results are satisfactory.



V Lymphosarcoma of the Orbit



VI Retinoblastoma

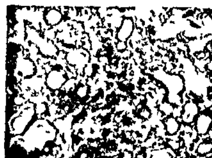
LYMPHOMA

Lymphoma may be benign or malignant and it may be associated with leucaemic blood picture. Nine cases could be followed up from the series of fourteen. Two cases later on showed typical leucaemic blood picture and died. Two other cases showed malignant character in later biopsies. So in benign lymphoma repeated biopsies and blood count are necessary. Five patients are doing well at present after irradiation therapy.

LYMPHOSARCOMA

Seven of the present series of ten lymphosarcoma showed localised lesions in the orbit. Three patients with generalised metastasis died within a year. Three other patients are doing well for nearly three years after surgery and radio therapy. Two patients refused operation but were given irradiation therapy and are known to have died after multiple manifestations. No follow up data was available in other two cases.





I Mixed Tumour of the lacrimal gland





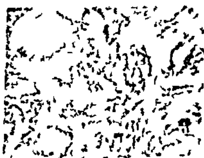
II Dermoid Cyst of the Orbit

DERMOID CYST

All the present fifteen cases of dermoid cysts of the orbit were noted in the second and third decades of life

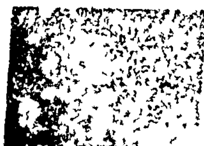
The usual treatment of complete operative removal was adopted in all cases and there was no recurrence





III Haemangioma of the Orbit





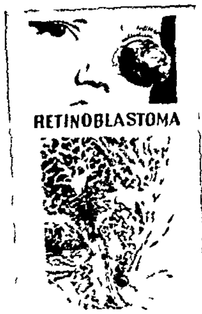
IV Lymphoma of the Orbit

HAEMANGIOMA

Twelve of the fourteen cases of haemangioma of the orbit were of cavernous variety Surgical removal and irradiation were the two methods of treatment adopted Observing the complications of irradiation in two cases surgical removal was employed in twelve cases and the results are satisfactory



V Lymphosarcoma of the Orbit



VI Retinoblastoma.

LYMPHOMA

Lymphoma may be benign or malignant and it may be associated with leucaemic blood picture *Nine cases could* be followed up from the series of fourteen Two cases later on showed typical leucaemic blood picture and died Two other cases showed malignant character in later biopsies So *in benign lymphoma* repeated biopsies and blood count are necessary *Five patients* are doing well at present after irradiation therapy

LYMPHOSARCOMA

Seven of the present series of ten lymphosarcoma showed localised lesions in the orbit Three patients with generalised metastasis died within a year Three other patients are doing well for nearly three years after surgery and radio therapy Two patients refused operation but were given irradiation therapy and are known to have died after multiple manifestations No follow up data was available in other two cases

II Intraocular Tumours

160 cases of intraocular tumours were examined histopathologically (Table No II) Of these 148 cases were retinoblastoma

TABLE II — *Intraocular Tumours*

Lists

1	Retinoblastoma	148
2	Malignant melanoma of Choroid	5
3	Haemangioma of Choroid	3
4	Leucaemia	2
5	Malignant Melanoma of Ciliary Body	1
6	Metastatic Carcinoma of Choroid from breast	1
	Total	160

RETINOBLASTOMA

The average age of the present series of cases was 3 8 years The oldest one was 20 years and the youngest one was one month old The disease was bilateral in 29% of cases All cases were sporadic except one where patient's mother was a retinoblastoma survivor Three instances of familial incidence were noted in this series and in





VII Epithelioma of the Lid





VIII Papilloma of the Lid

one family none of the five children survived from retinoblastoma, although the parents were free from the disease Histologically, rosette formation was noted in 68% cases and optic nerve extension was observed in 44% cases The tumour possesses a poor prognosis 37 bilateral cases could be followed up and none of them is known to have survived Only 14 cases are known to be living at present from the 86 unilateral follow of cases Spontaneous regression was noted in two cases where the eyes resulted in phthisis bulbi

III Tumours of the Lids

Out of 170 cases of tumours of the lid, the common tumours are (Table III) —

TABLE III — *Tumours of the lids*

1	Epithelioma	52
2	Haemangioma	32
3	Papilloma	17
4	Fibroma	15
5	Dermoid	14
6	Naevus (Melanotic)	10
7	Lipoma	7
8	Sarcoma	6
9	Adenoma of sebaceous gland	3
10	Adenocarcinoma of Meibomian gland	3
11	Malignant Melanoma	3
12	Lymphoma	2
13	Lymphosarcoma	2
14	Neuroma	2
15	Ad noma of Meibomian gland	1
16	Adenocarcinoma of sw at gland	1
	Total	170

1 Epithelioma
2 Haemangioma
3 Papilloma
4 Dermoid
5 Fibroma

EPITHELIOMA

Of the 52 cases of epithelioma of lids 46 were basal cell variety and the rest were squamous cell variety Only two cases came in the late stage where there were invasion of the lids conjunctiva and the orbit One of them is known to have died and the other symptom free now The usual treatment adopted in all cases was complete and wide excision followed by irradiation Special care was taken in determining the extent of the lesion and the excision was done beyond the site of the

lesion In the majority of the cases lower lids were affected and this was helpful in the plastic repair

PAPILLOMA

Papillomas are benign, but rarely may undergo malignant change One of the present 17 cases was malignant (early stage) Good result was obtained by simple excision of the tumour Another one of these cases showed recurrence, but this was not followed by malignant change

FIBROMA

Excision was the treatment No recurrence or the malignant change was observed in the present 15 cases

Haemangioma and the dermoid have already been discussed in connection with the orbital tumours

IV Epibulbar Tumours

The common epibulbar tumours from the present observation of 154 cases are as follows (Table No IV)

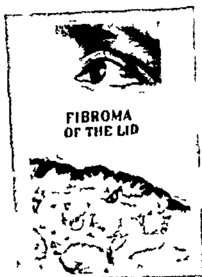
TABLE IV — *Epibulbar Tumours*

Lists

(i) Dermoid	28
(ii) Epithelioma	27
(iii) Haemangioma	23
(iv) Fibroma	22
(v) Papilloma	16
(vi) Naevus	15
(vii) Lipoma	9
(viii) Lymphoma	5
(ix) Adenoma	4
(x) Malignant Melanoma	3
(xi) Sarcoma	1
(xii) Teratoma	1
Total	154

1 Dermoid
2 Epithelioma
3 Haemangioma
4 Fibroma
5 Papilloma

All these tumours have already been discussed in connection with the tumours of the orbit and the tumours of the lids



IX. Fibroma of the Lid

V Tumours of the Lacrimal Passages

The only tumour noted in this connection was a carcinoma of the lacrimal sac

COMMENT

Tumours of the eye is a vast subject but when the tumours of the different sites are considered together, many tumours are found to be common and the subject then appears easier

Although the list of orbital tumours is large the common tumours form the majority of the cases From the clinical point of view the subject can be made simpler if the tumour is called by its basic name and not by the various descriptive terms For example for mixed tumour of the lacrimal gland there are such names as adenocarcinoma, cylindroma adenoid cystic epithelioma myxo-chondrocarcinoma and adenoma The treatment of the different orbital tumours depends on the correct diagnosis For instance for mixed tumour of the lacrimal gland treatment is radical surgery followed by post operative deep X ray therapy for lymphoma and lymphosarcoma deep X ray therapy for haemangioma, surgery or deep X ray therapy

Retinoblastoma is not only the commonest intraocular tumour but also the most common tumour of the eye in the present observation Only 14 cases from the present series of 148 retinoblastoma are living at present. The poor result of the present observation was due to delay in coming in the early stage of the disease high incidence of bilaterality early metastasis particularly tumour extension via the optic nerve even before the appearance of proptosis

Epitheliomas of the lids and epibulbar regions possess a good prognosis Only one case from the present series of 79 epitheliomas is known to have died This satisfactory result of the present observation was due to early diagnosis, complete and wide excision of the tumour and the post operative deep X-ray therapy

SUMMARY

650 cases of tumours of the eye were examined histopathologically in the pathology department of the Institute of Ophthalmology Calcutta (INDIA) over a period of 12 years The common tumours have been briefly discussed

ACKNOWLEDGEMENT

I am indebted to Prof K L Sen, Director, Institute of Ophthalmology, Calcutta for the encouragement in writing this paper and the kind permission for publishing the same I am grateful to Dr P K Sarkar, Pathologist and to Mr A Das Gupta, Artist for all possible help in this paper

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3 Das S P 1961 *J all India ophthal soc*, **9** 30
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5 Duke Elder 1938 Text Book of Ophthalmology Vol 2 *Henry Kimpton* London P 1775
6 Duke Elder 1940 Text Book of Ophthalmology Vol 3 *Henry Kimpton* London P 2446
7 Duke Elder 1952 Text Book of Ophthalmology Vol 5 *Henry Kimpton* London P 4761
8 Ewing J E 1942 Neoplastic disease 4th ed *Philadelphia* W B Saunders Co
9 Forrest, A W 1949 *Arch of ophthal* **41** 198
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13 Martin, H E 1939 *Arch of ophthal* **22** 1
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15 Moore R A 1951 A Text Book of Pathology, 2nd ed *Philadelphia* W B Saunduco
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17 Reese A B 1953 Tumours of the Eye Haeber, New York
18 Reese, A B 1956 *Amer j ophthal*, **41**, 3
19 Sussman W 1922 *Brit j ophth* **22** 722
20 Willis R A 1948 Pathology of Tumours St Louis *C I Mosby Co*

LIST OF BOOKS EXHIBITED AT THE XIXth INTERNATIONAL CONGRESS OF OPHTHALMOLOGY—DONATED TO THE ALL INDIA OPHTHALMOLOGICAL SOCIETY

	Name of the Book	*Author*	*Published by*
1	Glaucoma	Dr Sidney Lerman	Messrs Charles C. Thomas U S A
2	Night Vision	Dr Jayle Gaetan E	do
3	Optics	Dr Kenneth N Ogle	do
4	Atopic Cataract	Dr Emanuel Rosen	do
5	Principles of Ophthalmology	Dr John H Erbaugh	do
6	The Aqueous Veins	Dr Karl W Ascher	do
7	Eye Signs in General Disease	Dr F Herbert Hoessler	do
8	Geographic Ophthalmology	Dr Holmes	do
9	Clinical Electro-retinography	Dr Jerry Hart Jacobson	do
10	The Transparency of the Cornea	—	Messrs Blackwell Scientific publications Ltd Oxford
11	Lecture notes on Ophthalmology	Dr Patrick D Trevor Roper	do
12	Biochemistry of the Eye	Dr Antoinette Pirie & Dr Rum Van Heyningen	do
13	Glaucoma	—	do
14	Endogenous Inflammations of the Uveal Tract	Dr Alan C Woods	Messrs Baillière Tindall and Cox Ltd London
15	Clinical Neuro-ophthalmology	Dr Frank D Walsh	The Williams and Wilkins Co U S A
16	Medical Dictionary	Stedman	do
17	The Structure of the Eye	Dr George K. Smelser	Messrs Academic Press Inc London
18	The Eye—Ist volume	Dr Hugh Davson	do
19	System of Ophthalmology (Vol VII)	Sir Stewart Duke Elder	Henry Kimpton London
20	Ophthalmologic Diagnosis	F Herbert Hoeller	—
21	Ocular Allergy	Dr Frederick H Theodore & Dr Abraham Schlossmann	—

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20 Willis, R A 1948 Pathology of Tumours St Louis *C V Mosby Co*

Name of the Book	*Author*	*Published by*
41 TRANSACTIONS OF THE OPHTHALMOLOGICAL SOCIETY OF THE U K (Vol LXXXI)	—	J & A. Churchill Ltd London
42 OPHTHALMIC NURSING	Dr Maurice Whiting	do
43 AN ATLAS OF THE DISEASES OF THE EYE	Dr E S Perkins & Dr Peter Hansell	do
44 TEXT BOOK OF THE FUNDUS OF THE EYE	Dr Arthur J Ballantyne & Dr I C. Michaelson	Messrs E & S Livingstone Edinburgh
45 EYE SURGERY	Dr H B Stallard	Messrs John Wright & Sons Ltd
46 THE PRESERVATION OF EYE SIGHT	Sir Arthur Salisbury & Dr McNalty	do
47 A SYNOPSIS OF OPHTHALMOLOGY	Dr J L C Martin Doyle	do
48 THE EYE (Vol II)	Dr Hugh Davson	—
49 THE EYE (Vol III)	Dr Hugh Davson	—
50 THE EYE (Vol IV)	Dr Hugh Davson	—
51 ALMANACH FUR DIE AUGENHEILKUNDE 1960	Dr J F Lehmanns Verlag Monchen	—
52 DIE BEHANDLUNG DES SCHIELENDEN KINDES	Dr J F Lehmanns Verlag Monchen	—
53 MEDIZINISCH TECHNISCHE ARBEIT A UGEN LABORATORIUM	Dr E Wellmann	—
54 PRINCIPLES OF OPTICS AND REFRACTION	Prof L. P Agarwal	Medical publications Delhi
55 AUGENDIENST THE SERVICE OF THE EYES	Dr George Bartisch	Messrs Laboratorios Del Norte De Espana S A of Masnou (Barcelona) Spain
56 TESTS FOR COLOUR BLINDNESS	Dr S Ishihara	Kanehara Shuppan Co Ltd Tokyo Kyoto Japan

	Name of the Book	Author	Published by
22	Slitlamp Gonioscopy (Edn II)	Dr George Gorin & Dr Adolf Posner	Messrs Baillière, Tindall & Cox Ltd London
23	Principles and Practice of Optical Dispensing and fitting	Dr L S Sasieni	—
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28	Antibiotics and Sulphanomides in Ophthalmology	Dr Arnold Sorsby & Dr Joseph Ungar	Messrs Oxford University Press Bombay
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34	Squint—the Binocular Reflexes and the Treatment of Strabismus	Dr Keith Lyle & Dr C J O Bridgeman	do
35	Ophthalmic Operations	Dr Phillips & Foster	do
36	Applied Physiology of the Eye	Dr H Willoughby Lyle	do
37	Ophthalmology in Tropics	Dr E J Somerset	do
38	May & Worth s Manual of Diseases of the Eye (Edn XII)	Dr T Keith Lyle & Dr A G Cross	Messrs Baillière Tindall & Cox Ltd London
39	Uveitis and Toxoplasmosis	Dr E S Perkins	do
40	Parsons Diseases of the Eye	Sir Stewart Duke Elder	J & A Churchill Ltd London

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41 Transactions of the Ophthalmological Society of the U K (Vol LXXXI)	—	J & A Churchill Ltd London
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49 The Eye (Vol III)	Dr Hugh Davson	—
50 The Eye (Vol IV)	Dr Hugh Davson	—
51 Almanach Fur Die Augenheilkunde 1960	Dr J F Lehmanns Verlag Monchen	—
52 Die Behandlung des Schielenden Kindes	Dr J F Lehmanns Verlag Monchen	—
53 Medizinisch Technische Arbeit A Ugen Laboratorium	Dr E Wellmann	—
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55 Augendienst the Service of the Eyes	Dr George Bartisch	Messrs Laboratorios Del Norte De Espana S A of Masnou (Barcelona) Spain
56 Test for Colour Blindness	Dr S Ishihara	Kanehara Shuppan Co Ltd Tokyo Kyoto Japan

FILMS EXHIBITED AT THE XIXth INTERNATIONAL CONGRESS OF OPHTHALMOLOGY—1962

3rd December 1962

Callahan, A (U S A)	Symposium on entropion surgery for different types
Hughes W L (U S A) and Orkan *G Stasior*	Techniques of obtaining fascia lata for grafting
Hikaru H (Japan)	Automatic recording of visual acuity in vision testing
Fox S A (U S A)	Senile entropion surgical correction
Shigehisa Okamura (Japan)	A new surgery against obstruction of *nasolacrimal duct with or without* dacryocystitis
Rais Hadi (Tunesia)	Lamellar Keratoplasty in corneal fistula
Barraquer, J (Colombia)	Experimental refractive surgery
Marcel Noix (France)	Etude dynamique direct et radiologique de differents phenomenas oculaires
Gunther, G (W Germany)	Objective determination of visual acuity

4th December 1962

Castroviejo R (U S A)	Instrumentations techniques and results in keratectomies
Cooper S N (India)	*Circular guide and knife*
Hervouet F (France)	Les tatuages de la cornie
Casonavas J (Spain)	Fleringa's ring and its modification
Gupta U C (India)	*Trachoma*

5th December 1962

Landegger C P (U S A)	*Filaria loa of the eye*
Schimek R A (U S A)	Use of air in cyclodialysis clefts
Sinskey R M (U S A)	A surgical procedure for the improvement of congenital nystagmus
Agarwal L I (India)	Retinitis pigmentosa – a new therapeutic *approach*
Chandra D B (India)	Cataract extraction a modified technique
Suzumura A (Japan)	New measurement apparatus of accommodation (An H S Autograph asthenopia meter
Eusebio J (Philippines)	Scleral transposition in selected disease of the optic nerve and retina

Hagino R (Japan)	New measurement apparatus of accommodation (H S Autographic asthenopia meter)
Draeger J (W Germany)	Clinical tonography
Kara G B (U S A)	Penetrating keratoplasty in aphakia
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SYMPOSIUM IV

PROBLEMS RAISED IN OPHTHALMOLOGY BY THE RECENT PROGRESS IN AVIATION

VISUAL ACUITY AND OCULAR MUSCLE BALANCE REQUIREMENTS IN MODERN AVIATION

By Wing Commander T G JONES

India

INTRODUCTION

Every conscious moment we are constantly fed by our eyes with information as to the nature of objects in our environment and as to their location in space The first is the function of visual acuity, the second of depth perception The piloting of high performance aircraft require a high performance of both these functions I will briefly review the qualities of these functions that are required for in jet age pilots and will discuss whether the present day standards and the ophthalmic examination in routine use to ensure the fulfil ment of these standards meet these requirements in the light of experience in the Indian Air Force

VISUAL ACUITY

Out of Nicholl's[26,27,28] comprehensive study on the relation ship of heterophoria to depth perception in aviation, the one very definite fact that emerged was the co relation between visual acuity and flying performance The high altitudes and the high speeds attained by present day aircraft adversely influence the pilot's visual acuity efficiency

At high altitudes the flyer is frequently faced with an empty visual field Whiteside's[37,38] investigation on the effect of this empty visual field on visual performance reveal that under these conditions, the emmetropic eye seems to rest on an accommodation level of + 0 6 D, this may be boosted upto + 1 5 D by the pilot's efforts to search for his target The resulting myopia doubles the minimum visual angle thereby reducing pick up range to half the normal Target detection is further hampered by the lack of sufficient contrast between the object and its surroundings The absence of any back ground to provide parallactic displacement renders movement discri mination and judgement very difficult

The pick up range is determined by the resolving power of the eye The higher the resolving power the greater the pick up range and the more time the pilot has at his disposal to decide upon and carry out a course of action This is amply illustrated in Table I on page 889

It must be appreciated that the images of objects first sighted usually first strike the peripheral retina which has a lower resolving power, requiring twice the foveal threshold size at 5 from the fovea,

and four times the foveal threshold size at 10° from the fovea The presence of a refractive error will considerably raise these thresholds

TABLE I *Pick up ranges for a fighter aircraft (fuselage diamension 84) and time intervals at 1800 m p h for various visual acuity levels*

Visual Acuity	*Pick up range (miles)*	*Time interval (in seconds)*
6/12	2 2 miles	4 4 secs
6/9	2 9 miles	5 9 secs
6/6	4 4 miles	8 9 secs
6/5	5 3 miles	10 7 secs
6/4	6 6 miles	13 3 secs

The speed of the visual perception is woefully inadequate to meet the demands of modern aircraft, and this combined with the difficulty of seeing at altitudes is a major factor in mid air collisions Byrnes [45] and Strughold [33 34] have shown that the small time intervals of the chain of latencies of visual perception assume importance in the background of the speeds attained by present day aircraft Table II, gives these time intervals and the distances covered during these intervals at speeds of 600 m p h and 1800 m p h

TABLE II —*Time intervals and distances travelled between first sighting an object and changes of flight paths (after Byrnes)*

Operation	*Time in seconds*		*Progressive distance travelled in feet*	
	For operation	*Progressive total*	*at 600 m p h 880 /sec*	*at 1800 m p h 2640 /sec*
I Perception and extra foveal to foveal perception (Minimum recognition)	1 045	1 045	924	2 759
II Decision and motor response	2 40	3 445	3 032	9 095
III Aircraft response	2 0	5 445	4 792	14 375

These time intervals are absolute minima and vary with the intensity and wave length of the stimulus, the region of the retina stimulated and its state of adaptation Any factor causing a fall in the

visual acuity, such as the refractive error, obstructions to vision, dirty windshields and visors acceleration forces, anoxia and fatigue will greatly stretch these time intervals

The total time interval from extra foveal perception to aircraft response is 5 445 secs Table I shows that with 6/9 vision, the pilot has a pick up range of 2 9 miles giving him 5 9 seconds at a closing speed of 1800 m p h , and so just meets these requirements Hence, it follows that the minimum uncorrected binocular vision for a pilot of present day aircraft should not be below this level Fast mechanical adjustment of the eyes should be included in the criteria for assignment to high speed aircraft, and the effects of age on the speed of these adjustments should also be taken into account

Much research effort has been expended to lessen the pilot s visual load and to make good his deficiencies — in many cases however this has merely resulted in the transfer of the visual task from outside to inside the cockpit and has created new problems

The use of radar requires the pilot or the navigator to observe very attentively at near distance, a fluorescent screen on which are brightening and fading aggregations of relatively dim points of lights on a dark background and to make a rapid and accurate interpretation of the display Gerathewohl [14] has determined that the eye movements in radar operations are complex and are carried out in jerks The duration of movement vary with the task from 20 to 25 ms The duration of fixation ranges from 430 ms for an orientation task to 1815 ms for a bombing task The straining of the eyes in this unusual manner may result in fatigue drowsiness, asthenopia and headaches

According to Bellecci [2] heterophoria, hypermetropia and mild anisometropia hinder visual performance and predispose to visual breakdown Riffenburgh [29] recommends that the radar operator should look away to relax his accommodation every third or fourth sweep

The change of fixation from scope to instrument panel and to outside the cockpit require the eyes to rapidly adapt through a wide variation of brightness levels According to Herrick and his co workers [15] aircrew viewing a C R T display experience a fall in visual efficiency impairing the ability to read instruments and to perceive objects external to the aircraft Efficient visual function under these conditions demand good near visual acuity with speedy accom modation speedy visual reactions and binocular vision at near distances

Since the wearing of correcting lenses by pilots of modern high speed aircraft is problematical and not accepted universally a high degree of uncorrected visual acuity is required to meet these demands Visual standards in the Indian Air Force have always demanded 6/6 vision in one eye and 6/9 vision in the other correctable to 6/6, manifest hypermetropia being limited to + 2 25 D

Analysis of 2,266 examinations conducted at the Central Medical *Establishment* [9] reveal that (79 8%) of candidates accepted under these standards have an unaided binocular vision of at least 6/5, thereby fully meeting the demands *of modern flying* *Of* the serving aircrew, ages ranging from 20 to 45 years reviewed, (84 1%) had unaided binocular vision of 6/5 and only 2 8% had unaided binocular vision lower than 6/12 — the extreme limit being 6/36 — 6/60, with a refraction of — 1 5 D

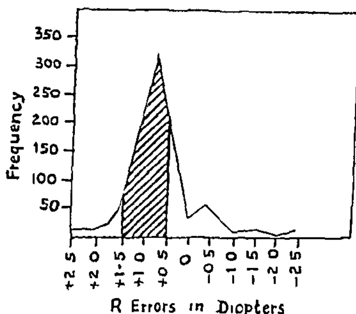


Fig 1

Distribution of refractive errors in accepted candidates and in serving aircrew

The distribution of the refraction in accepted candidates and in serving aircrew is shown in Fig 1 This shows that 80% have a refractive ranging from + 0 5 D to + 1 5 D This has two advantages *Firstly, this range of refraction neutralises the myopia of the empty* visual field and ideally suited for search at high altitudes Secondly, this range of refraction is sufficient to offset the myopic tendencies that occur between the 20 and 30 years, which, Diamond [8] and Howard [16] & Slapter [3] have estimated as an annual shift of — 0 05 D

Analysis of the refraction in relation to their visual acuity is shown in Table III on page 892

At the 6/6 level, the refraction may range from — 1 5 D to + 3 5 D The norm for myopia being — 0 5 D and that for hypermetropia + 0 75 D At the 6/9 level, the refraction range was from — 2 5 D to + 4 5 D The norm for myopia being — 0 75 D and that for hypermetropia *+ 1 5 D The inaccuracy of* visual require

TABLE III — *The limits of refractive errors encountered together with the mean and modal refraction at each visual acuity level*

Visual Acuity	Myopic limit	Hyper metropic limit	— Error		+ Error	
			Mean	Mode	Mean	Mode
6/5	−0 5D	+2 5D	−0 25D	−0 25D	+0 75D	+0 75D
6/6	−1 5D	+3 5D	−0 50D	−0 50D	+0 80D	+0 75D +1 0 D
6/9	−2 5D	+4 5D	−1 0 D	−0 75D	+1 24D	+1 25D +1 5 D

ments in terms of visual acuity alone without considering the refraction becomes evident Diamond[10] recommends that the requirement for airline pilots should be 6/6 vision with a refraction of not less than +0 5 D to neutralise the myopia shift of the 20–30 year range and not more than +1 0 D to offset any deterioration that might occur due to the pre presbyopic hypermetropic shift This will safeguard against the loss of experienced pilots due to acquired visual defects and will ensure a high standard of visual efficiency over a 10 to 15 year period This however is an ideal requirement a more practical approach demands further investigation to widen these limits

DEPTH PERCEPTION AND OCULAR MUSCLE BALANCE

No aspect of vision in aviation has been more extensively investi gated and has led to more diversity of opinion than depth perception and its relation to ocular muscle balance Experience in World War I showed that 70 to 80% of accidents were due to bad landings and according to Clements[7 8] these were mainly caused by hetero phoria made manifest by fatigue Howard[17 18 19] in an analysis of World War I accidents concluded that the judgement of distance was mainly dependent on good and equal vision in the two eyes, and that the main factor was binocular parallax This observation resulted in the Howard Dolman test which has ever since been used as a crite rion for the depth perception ability necessary for flying Ocular muscle imbalance was viewed with concern and Doyne[11] held that heterophoria often implied the unequal action of the extra ocular muscles resulting in a bilateral visual disharmony He considered a one eyed man with acquired stereoscopic vision less dangerous for flying than a two eyed man whose eyes may be unreliable These views resulted in very stringent standards for heterophoria being laid down at the Peace Convention in 1917 and agreed on for international use by the medical sub committee of the International Commission for Air Navigation at Rome in 1927 These prevailed upto the beginning of World War II

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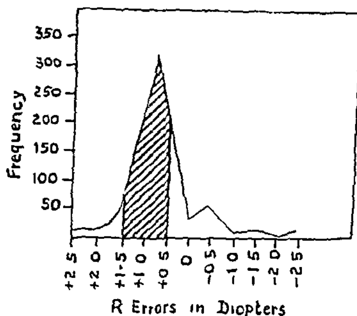


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6/9	−2 5D	+4 5D	−1 0 D	−0 75D	+1 24D	+1 25D +1 5 D

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In the Royal Canadian Air Force, from August, 1942 to October, 1944, 21.7% of candidates were rejected for ocular defects, at the recruiting centres, 4.5% were rejected for ocular muscle balance (Nicholls) [26, 8]. The need was, therefore, felt to determine the validity of the ocular muscle balance requirements. On evaluation, it was felt that binocular factors were of greatest value at relatively close range, and it was realised that some functions of depth perception, such as, the estimation of air speed and the determination of the effective range for gunfire were aided by mechanical devices, such as the air speed indicator, and the gunsight, thereby limiting the use of binocular factors in flying. This resulted in the adoption of more liberal standards in the Royal Canadian Air Force, demanding relatively lenient standards for new trainees and not requiring good binocular vision in experienced personnel with good flying records. When Kirschberg's [22] careful study in 1944 found no relationship between heterophoria, fusion, stereoptic acuity and flying performance, this approach was justified.

Various studies Berens [3], Duguet [12], Macfarland [23, 24], Neely [5], Velhagen [36] on the effect of anoxia on ocular muscle balance supported these revised standards, in so far as, stereopsis remained very resistant to the effect of anoxia, though the lateral phorias tended to increase and the convergence weaken. Moreover, since the adverse effects of anoxia were offset by the use of oxygen and with the advent of pressurised fuselages, ocular muscle balance limitations became unnecessary.

Nicholls [8] classified pilots into four distinct groups according to their ocular muscle balance and their landing capabilities.

Group I. Pilots with good ocular muscle balance, and who are good landers — the traditional ideal.

Group II. Pilots with good ocular muscle balance but who are poor landers — the cause lies with the faulty interpretation of the information obtained from the eyes.

Group III. Pilots with poor ocular muscle balance and who are good landers. These pilots have developed accurate monocular depth perception based on size, motion parallax and perspective.

Group IV. Pilots with poor ocular muscle balance and who are poor landers. This group comprises only 1% of all pilots and has two sub divisions —

(*a*) Good pilots who lose confidence due to stress or some minor flying accident. These benefit by rest and psychotherapy.

(*b*) Pilots who have never learnt to use monocular cues in landing. These may be helped by orthoptic exercises.

Based on these concepts, Nicholls [28] recommended that providing there is no frank diplopia there is no need for ocular muscle

balance restrictions for pilot duty, and that imbalance of longstanding resulting in neglect or suppression may be acceptable for flying This last is an extreme view and is controversial A pilot, with ocular neglect is restricted to a monocular field thereby limiting his chances of target detection Moreover, since motion parallax is a function of the peripheral retina the effect of the unequal temporal and nasal fields of monocular vision on motion parallax whilst landing should be fully evaluated before accepting this handicap

The evaluation of a single depth perception factor, as is done by the depth perception tests in current use, is not valid to assess or predict the complex function of spatial orientation The use of these tests as criteria of potential flying performance is not justified There is also no doubt that binocular cues are of little value as aids to flying Teichner and his co workers [35] find that they are slightly superior to the monocular cues only upto 1900 ft Rose[30] and Scobee[31] also find binocular cues widely overrated since the pilot's visual tasks are performed at distances at which binocularity makes little difference Evaluating the monocular cues Rose[30] finds that motion parallax and the size of retinal image are the main factors during flight and landing Cibis[6] finds linear perspective and the size of retinal image most important cues and that flying ability can be improved by training and does not rely upon a well developed sense of stereopsis

The piloting of aircraft through periscopes and closed circuit television is envisaged The problems attendant with this procedure are the maintenance of the convergence accommodation ratio the effect on distance judgement, of instrument minification, of the scope haze and of the apparent increase in the angular velocity of approaching objects caused from the difference between the pilot s eye position and the objective

In laying down standards there is a tendency to assume that if ocular muscle balance is normal it follows that the depth perception is adequate to meet the demands of flying Experience in the Indian Air Force justifies this view It is probable that the poor landers of Nicholls Group II and IV are either eliminated at the training stage or improve their depth perception as training and experience proceed

In Indian Air Force the limits of heterophoria are 6 0 p d of esophoria and exophoria and 1 0 p d of hyperphoria at 6 meters and 6 0 of esophoria 16 0 p d exophoria and 1 0 p d hyperphoria at 30 cms The main reason for these limitations is to ensure against decompensation in flight from fatigue and flying stresses With this object in view, the main weightage in routine ocular muscle balance tests for flying fitness should be given to the tests that evaluate the fusion sense In a review of ocular muscle balance tests performed on candidates for the Indian Air Force,[21] the incidence of the lateral phorias as determined by the Maddox Rod at 6 meters and 30 cms in 775 cases reviewed is indicated in Fig 2

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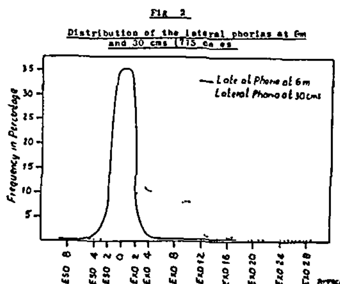


Fig 2
Distribution of the lateral phorias at 6 m and 30 cms (775 cases)

The curve of the lateral phorias at 6 meters shown are approximately normal distribution, peaking at 0 5 p d of esophoria and exophoria — 80 2% falling between 1 5 p d of esophoria and 1 5 p d of exophoria The curve for lateral phoria at 30 cms shows an uneven distribution, but (84 7%) fall between 1 p d and 10 p d of exophoria, indicating a shift towards exophoria at near distance This is because any deficit of the convergence required at 30 cms is manifested as an exophoria, (and so explains the very frequent association of bar responses in the Bishop Harman test and latent divergence on the near cover test with moderate esophoria at near distance) In no instance, did the Maddox rod tests give any indication of uniocularity, this was only revealed by the Bishop Harman and cover tests

Comparative values of objective convergence (C), subjective convergence (S C), and the SC — C difference in borderline and unfit cases are shown in Table IV

TABLE IV — *Average convergence values in borderline and unfit cases*

	No	*Obj Con (C) in cms*	*Subj Con (SC) in cms*	*SC — C in cms*
Binocular cases beyond Maddox rod limits	15	7 4	15 7	8 3
Uniocular cases (*a*) beyond Maddox rod limits	9	7 7	21 0	13 3
(*b*) within Maddox rod limits	12	8 0	18 8	10 8

It is evident that the larger SC — C differences are associated with uniocularity, and therefore the SC — C difference gives a good indication of the fusion sense The smaller the difference the better the fusion the larger differences, especially when associated with higher C values indicate poor fusion This is worthy of confirmation by further investigation since the test is a simple one requiring simple equipment and little skill

In our experience there has been no known case of a decompensation of heterophoria among aircrew, either from *flying stresses* or from any other reason The range of lateral phorias in 206 Air Force and air line pilots is shown in Table V

TABLE V — *Mean and Range of Lateral Phoria Values in serving aircrew (206)*

	Far	*Near*
Mean	*0 03* p d *Eso*	5 *69* p *d Exo*
95% range	2 0 p d Eso to 4 0 p d Exo	6 0 p d Eso to 16 0 p d Exo
Total Range	8 0 p d Eso to 18 0 p d Exo	8 0 p d Eso to 24 0 p d Exo

The extreme limit of exophoria 18 p d for far and 24 p d for near is represented by an airline pilot who is uniocular on the Bishop Harman with the cover test indicating alternating divergence, who was initially made fit when examining conditions were more lax He now has a good flying record of more than 5 000 hours to his credit

SUMMARY AND CONCLUSION

The piloting of high speed aircraft at high altitude demand a high degree of uncorrected visual acuity The visual standards prevalent in the Indian Air Force of 6/6–6/9 vision meets these requirements ensuring a binocular visual acuity of 6/5 in (79–8%) of the population accepted a refraction range, from + 0 5 to + 1 5 D in 80% of serving pilots which suits search under empty visual field conditions and which is a safeguard against the loss of visual efficiency due to acquired defects

It would be more accurate to combine the visual acuity level with limits of refraction The ideal range of refraction acceptable for initial trainees would be + 0 5 D to + 1 0 D, but to be practical, wider limits should be considered It would be advantageous to establish criteria for speedy visual perception in personnel assigned to high performance aircraft

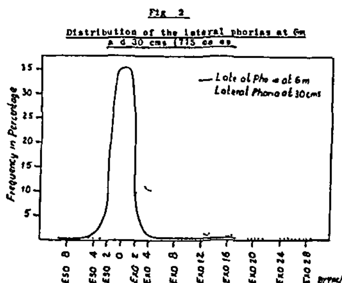


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TABLE V — *Mean and Range of Lateral Phoria Values in serving aircrew (206)*

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Mean	0 03 p d Eso	5 69 p d Exo
95% range	2 0 p d Eso to 4 0 p d Exo	6 0 p d Eso to 16 0 p d Exo
Total Range	8 0 p d Eso to 18 0 p d Exo	8 0 p d Eso to 24 0 p d Exo

The extreme limit of exophoria 18 p d for far and 24 p d for near is represented by an airline pilot who is uniocular on the Bishop Harman with the cover test indicating alternating divergence, who was initially made fit when examining conditions were more lax He now has a good flying record of more than 5 000 hours to his credit

SUMMARY AND CONCLUSION

The piloting of high speed aircraft at high altitude demand a high degree of uncorrected visual acuity The visual standards prevalent in the Indian Air Force of 6/6–6/9 vision meets these requirements ensuring a binocular visual acuity of 6/5 in (79·8%) of the population accepted a refraction range, from + 0 5 to + 1 5 D in 80% of serving pilots which suits search under empty visual field conditions and which is a safeguard against the loss of visual efficiency due to acquired defects

It would be more accurate to combine the visual acuity level with limits of refraction The ideal range of refraction acceptable for initial trainees would be + 0 5 D to + 1 0 D but to be practical wider limits should be considered It would be advantageous to establish criteria for speedy visual perception in personnel assigned to high performance aircraft

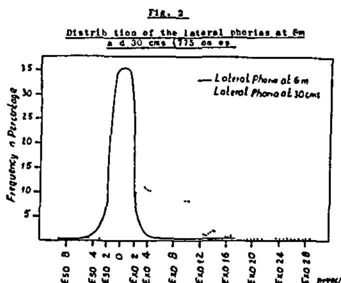


Fig. 2
Distribution of the lateral phorias at 6 m and 30 cms (775 cases)

The curve of the lateral phorias at 6 meters shown are approximately normal distribution, peaking at 0.5 p.d. of esophoria and exophoria — 80.2% falling between 1.5 p.d. of esophoria and 1.5 p.d. of exophoria. The curve for lateral phoria at 30 cms shows an uneven distribution, but (84.7%) fall between 1 p.d. and 10 p.d. of exophoria, indicating a shift towards exophoria at near distance. This is because any deficit of the convergence required at 30 cms is manifested as an exophoria, (and so explains the very frequent association of bar responses in the Bishop Harman test and latent divergence on the near cover test with moderate esophoria at near distance.) In no instance, did the Maddox rod tests give any indication of uniocularity, this was only revealed by the Bishop Harman and cover tests.

Comparative values of objective convergence (C), subjective convergence (S.C.), and the SC — C difference in borderline and unfit cases are shown in Table IV.

Table IV. — *Average convergence values in borderline and unfit cases*

	No.	*Obj. Con. (C) in cms.*	*Subj. Con. (SC) in cms.*	*SC — C in cms.*
Binocular cases beyond Maddox rod limits	15	7.4	15.7	8.3
Uniocular cases (*a*) beyond Maddox rod limits	9	7.7	21.0	13.3
(*b*) within Maddox rod limits	12	8.0	18.8	10.8

It is evident that the larger SC — C differences are associated with uniocularity and therefore the SC — C difference gives a good indication of the fusion sense The smaller the difference the better the fusion the larger differences, especially when associated with higher C values indicate poor fusion This is worthy of confirmation by further investigation since the test is a simple one requiring simple equipment and little skill

In our experience there has been no known case of a decompensation of heterophoria among aircrew, either from flying stresses or from any other reason The range of lateral phorias in 206 Air Force and air line pilots is shown in Table V

TABLE V — *Mean and Range of Lateral Phoria Values in serving aircrew (206)*

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The piloting of high speed aircraft at high altitude demand a high degree of uncorrected visual acuity The visual standards prevalent in the Indian Air Force of 6/6–6/9 vision meets these requirements ensuring a binocular visual acuity of 6/5 in (79·8%) of the population accepted a refraction range, from + 0 5 to + 1 5 D in 80% of serving pilots which suits search under empty visual field conditions and which is a safeguard against the loss of visual efficiency due to acquired defects

It would be more accurate to combine the visual acuity level with limits of refraction The ideal range of refraction acceptable for initial trainees would be + 0 5 D to + 1 0 D but to be practical wider limits should be considered It would be advantageous to establish criteria for speedy visual perception in personnel assigned to high performance aircraft

A very fine degree of depth perception is required to land high speed aircraft This ability bears no relation to heterophoria, nor can it be evaluated by any single depth perception test, it can be improved by training The most important monocular cues in flight and landings are *motion parallax*, retinal image and linear perspective

Though binocular cues only operate at limited distances, good binocular vision is necessary to provide a potentially wider visual field for target detection and for visual tasks within the cockpit, such as the efficient viewing of C R T displays Hence, the main objective of the ocular muscle examination of aircrew should be to establish the presence of binocularity with good fusion to ensure against decompensation in the face of flying stresses

Of the routine ocular muscle balance tests, only the Bishop Harman test and the cover test reveal uniocular tendencies, and that the difference between the subjective and the objective convergence is an excellent indication of the quality of the fusion sense In the evaluation of flying fitness, if due weightage is given to these tests, the ocular muscle balance requirements for modern flying will be fully met

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EALES S DISEASE—HISTORICAL REMARKS

M J ROPER HALL

Birmingham England

Henry Eales was born in 1852—25 years later in 1877 he was appointed surgeon at the Birmingham Eye Hospital and in 1880, published a paper in the Birmingham Medical Review entitled ' Cases of retinal haemorrhage associated with epistaxis and constipation" The following year he read a paper on the same subject of primary retinal haemorrhage in young men at the International Medical Congress in London

At the end of his career he was described as a man of singularly amiable character to whom his colleagues were sincerely attached He died in 1913 while holding the appointment of Senior Surgeon to the Birmingham Eye Hospital In his obituary notices attention was drawn to his publications on the state of the retina in 100 cases of granular kidney on uniocular retinitis albuminurica, on toxic amblyopia on causes and treatment of convergent squint and on paralysis of convergence and accommodation but no mention was made of his papers on the disease which bears his name and which forms the subject of the Symposium at this International Congress

CLINICAL FINDINGS

In his two papers on this subject he makes the points that the left eye was primarily and chiefly affected that vitreous haemorrhage is recurrent the vessels of the retina are found to be large and tortuous especially the veins that the haemorrhages were usually confined almost entirely to the periphery of the retina only occasionally being found round the disc and the macular area was not involved in any case The extravasations were almost invariably large, round or irregular and could often be seen to have proceeded from venou radicles which were obscured by them All his cases were young men between 14 and 20 years of age all had been subject to epistaxis especially during the Summer months, and all had been much troubled with constipation for some two to three years In all cases the pulse was habitually under 60 per min, but easily excited to rapidity In acknowledging the rarity of the condition he pointed out that by chance some four cases had come to his attention within a short period and that in the following year—although 12 000 out patients were treated at our hospital—not a single fresh case was seen He considered it remarkable that no case had been seen in a female and wondered whether the menstrual function was a safeguard

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LES PROBLEMES OPHTALMOLOGIQUES POSES PAR L ENVIRONNEMENT AU COURS DU VOL SPATIAL

A MERCIER[1] et G PERDRIEL[2]

(*Tours France*)

Quittant la terre pour l espace l astronaute enferme dans sa capsule, se trouve transporte dans un milieu nouveau auquel son organisme doit s adapter De meme que toutes ses fonctions sensorielles, sa vision subira les effets de cet environnement inhabituel qui en medecine de l espace, constitue l agent stressant principal

Nous avons utilise pour cette étude les renseignements recueillis lors des vols des cosmonautes americains et sovietiques

Nous envisagerons successivement l influence sur la fonction visuelle deux sortes d environnement

1 l environnement exteneur a la capsule
2 l environnement interieur a la capsule

I *I environnement exterieur*

Les *accelerations* qui surviennent lors de la mise a feu de la fusee porteuse atteignent des taux susceptibles d alterer la vision Lors des vols de Shepard et Grissom l acceleration de depart passa de 1 G a 6 3 G en 2 minutes elle fut de 6,7 G dans le vol de Glenn pour atteindre 7 7 G dans les 2 minutes suivantes Aucune alteration visuelle ne fut signalee a cette occasion

Par contre les vibrations qui lors du vol de Shepard apparurent une minute apres le lancement et au passage de la zone transsonique provoquerent l entree en vibration de la tete de l astronaute dont la vision fut momentanement brouillée les aiguilles des cadrans de bord ayant une apparence floue Ce trouble fut de tres courte duree, car 1 25 m apres le lancement Shepard etait capable de lire et de transmettre au sol les indications concernant la pression a l interieur de la cabine Des perfectionnements techniques ont d ailleurs reduit la frequence et l amplitude de ces vibrations lors des vols suivants et fait disparaitre leur repercussion sur la vision

C est lors de la re entree dans l atmosphere que les forces d acceleration atteignent leur valeur maxima en passant de 0 05 a 11 G en 31 secondes A ce moment les fonctions visuelles demeurerent normales et les cosmonautes n eprouverent pas de reduction du champ

[1] Chairman of the Vision Committee Aero Space Medical Panel AGARD NATO

[2] Médecin Commandant Professeur Agrege de Service de Santé de l Air

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visuel peripherique ni de "gray-out" De meme, lors du deploiement du parachute, une pointe a 4 G n'entraina aucun trouble visuel Les accelerations lineaires de depart et de re entree n'ont donc, au point de vue oculaire, rien provoque de plus que les reactions constatees lors des essais en centrifugeuse pour des valeurs de G correspondantes

Le vol spatial introduit la notion de la 3eme dimension de l'espace et l'astronaute doit pouvoir controler non seulement l'altitude, mais egalement le profil vertical et l'orientation geographique Les rotations successives de la capsule au cours du vol et les types inhabituels d'accelerations angulaires agissant a la fois sur la vision et les canaux semi circulaires peuvent provoquer la *desorientation* C'est ainsi que Grissom a pu eprouver une breve sensation de chute lors de la separation de la fusee porteuse et le sentiment de filer en arriere a la mise a feu des retro fusees L'entrainement qui a eduque l'astronaute a ne plus accorder foi qu'aux seules indications de ses instruments en negligeant ses propres sensations visuelles et cenesthesiques, semble avoir considerablement attenue sinon supprime cette cause d'erreur humaine

La pesanteur peut etre consideree comme le principal element de l'environnement exterieur car notre corps, au point de vue anatomique et physiologique, est, dans la vie terrestre, constamment controle par la pesanteur Or, au cours du vol spatial, lorsque la force d'attraction de la terre est contrebalancee par la force centrifuge du vehicule, il en resulte un etat de sub puis d'a pesanteur qui modifie completement notre equilibre habituel

L'etude du comportement de l'homme en *l absence d pesanteur* avait donne lieu a de nombreuses experiences preliminaires rendues difficiles du fait de difficulte de realiser artificiellement a proximite de la terre la suppression de la pesanteur pendant un certain laps de temps Les constatations faites lors des vols de l X 15, les experiences de Whiteside sur un sujet immerge, avaient indique que l'homme manifestait une incoordination psycho motrice transitoire lors du passage d un taux eleve de G a 0 G Whiteside avait montre que, lorsque la valeur de G passait de 1 à 0, l'objet fixe par le sujet semblait etre plus bas qu en realite alors qu au contraire l'objet semblait s'elever par rapport au sujet pour une valeur de 2 G Dans un film sovietique realise lors de l'envoi d un chien dans une fusee spatiale, Kousnetsov avait pu constater, lors du passage en a pesanteur, la deviation vers le bas des yeux de l'animal dont la tete avait ete maintenue immobile en la fixant avec du platre

Il est possible qu'une alteration du tonus musculaire soit a l'origine de ces deviations Les auteurs sovietiques (S V Ugau) ont en effet indique que si l on mesure la force musculaire d un sujet en etat de pesanteur puis d'a pesanteur, on la voyait souvent passer de 45/60 kgs a 4/5 kgs

L'analyse des mouvements des yeux de Shepard enregistres par la camera placee dans la capsule a permis de verifier si, durant les

diverses phases du vol, son attention s etait toujours dirigee correctement vers les instruments qu il devait controler

C est ainsi que, pendant les 20 premieres secondes il regarda la zone 9 du tableau de bord ou se trouvaient les signaux lumineux indiquant le bon fonctionnement du lancement ou l obligation d ejecter la capsule (Ready or Mayday) Durant le reste de la periode de lancement son regard observa les differentes zones contenant les indications concernant l altitude, l acceleration le tangage la pression cabine le carburant et l oxygène Durant l a pesanteur, les zones 6 7 8 furent les plus observees (Attitude de la capsule, heure periscope) Lors de la re entree, le regard fut surtout fixe sur la zone 4 controlant l acceleration durant la phase de la plus forte valeur de G et la zone 8 contenant le periscope qui servit a verifier le bon developpement du parachute

Ce film a demontre qu en toutes circonstances et notamment durant l absence de pesanteur le regard fut toujours correctement dirige sur les instruments appropries sans qu il apparaisse aucune trace d incertitude ou d incoordination dans les mouvements oculaires, de fixite intempestive ou de nystagmus I astronaute put toujours effectuer en temps voulu les divers mouvements commandes par les indications perçues visuellement sur le tableau de bord

Les renseignements recueillis lors du vol de Shepard, dont le sejour en a pesanteur n a guere depasse 5 minutes, ont ete confirmes par les vols suivants de Glenn (4 heures 30 d a pesanteur), Titov (25 heures) et enfin Popovich (71 heures) et Nicolaiev (94 heures) L absence de pesanteur ne provoque pas de troubles visuels Les observations speciales faites à ce sujet par Glenn a l aide d optotypes et d un oculogyric test ont prouve que la vision et la motilite oculaire demeuraient normaux

Bien que la capsule spatiale soit hermetiquement close un hublot permet l observation exterieure en dehors du periscope Lorsque la rotation de la capsule dirige cette ouverture en direction du soleil *l eblouissement* devient intense Cet eblouissement est d autant plus vif qu en tres haute altitude le bleu du ciel devient de plus en plus sombre Les travaux de White Riley et Jorve ont montre que la lecture des instruments de bord etait influencee par l association de l eblouissement et de l accéleration Au taux le plus elevé de brillance (42 milli lambert) il n existe pa de difference dans le pourcentage d erreurs commises aux differentes valeurs de G Au taux de brillance le plus bas la frequence des erreurs est en raison inverse de la brillance et en rapport direct avec la valeur de G A4 G il y a une augmentation systematique du pourcentage d erreurs lorsque la brillance diminue

Si tous les astronautes americains ou sovietiques ont signale l eblouissement intense survenant lors de l exposition du hublot en *direction du soleil* aucune indication n a ete donnee concernant la perturbation visuelle ayant pu en resulter à part les frequentes modifications de l adaptation rétinienne

visuel périphérique ni de “ gray-out ” De même, lors du déploiement du parachute, une pointe à 4 G n'entraîna aucun trouble visuel Les accélérations linéaires de départ et de re-entrée n'ont donc, au point de vue oculaire, rien provoqué de plus que les réactions constatées lors des essais en centrifugeuse pour des valeurs de G correspondantes

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L'étude du comportement de l'homme en *l'absence de pesanteur* avait donné lieu à de nombreuses expériences préliminaires rendues difficiles du fait de difficulté de réaliser artificiellement à proximité de la terre la suppression de la pesanteur pendant un certain laps de temps Les constatations faites lors des vols de l'X 15, les expériences de Whiteside sur un sujet immergé, avaient indiqué que l'homme manifestait une incoordination psycho motrice transitoire lors du passage d'un taux élevé de G à 0 G Whiteside avait montré que lorsque la valeur de G passait de 1 à 0, l'objet fixé par le sujet semblait être plus bas qu'en réalité alors qu'au contraire l'objet semblait s'élever par rapport au sujet pour une valeur de 2 G Dans un film soviétique réalisé lors de l'envoi d'un chien dans une fusée spatiale, Kousnetsov avait pu constater, lors du passage en apesanteur, la déviation vers le bas des yeux de l'animal dont la tête avait été maintenue immobile en la fixant avec du plâtre

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L'analyse des mouvements des yeux de Shepard enregistrés par la caméra placée dans la capsule a permis de vérifier si, durant les

et du vetement qui est d environ 14,7 livres par square inch lors du lancement passe a 5,7 apres une minute et demie et est maintenu a ce taux pendant toute la duree du vol jusqu à une reprise de la pressurisation a 25 000 pieds lors de la descente apres ouverture des parachutes

La temperature a l interieur de la cabine et du vetement doit etre egalement maintenue a des taux permettant un bon equilibre physiologique Elle varie d environ 15 lors du depart et de la descente et aurait ete maintenue entre 14 et 24 C (58 F et 76 F) pendant toute la duree des vols de Nikelaiev et Popovich Glenn cependant se plaignit d une transpiration abondante durant les dernières phases de sa descente et de sa recuperation

L humidification de l air dans la capsule joue un role aussi important que la temperature etant donne les relations qui existent entre ces deux elements C est ainsi que l addition d une humidite de 10% a une temperature seche de 70 F fait passer cette derniere a 63 F et qu une humidite de 70% produit, pour la meme temperature seche de 70 F un abaissement a 67 F Les experiences preliminaires aux divers vols spatiaux avaient montre que la temperature ne devait pas depasser 90 a 95 F (32 a 35 C) pour permettre l execution normale des diverses taches incombant a l astronaute

Le souci d eviter les erreurs que pourraient provoquer des perturbations oculo motrices du fait des accélérations ou de l a pesanteur a fait repartir les multiples *cadrans et instruments de bord* de façon a reduire l amplitude des mouvements oculaires du pilote L analyse du film de Shepard avait en effet montre qu etant donne la frequence du regard entre l indicateur de G et celui de carburant, il etait indispensable de reduire la distance separant ces deux cadrans

Les gaz nocifs depuis l oxyde de carbone jusqu aux fumees et vapeurs irritantes peuvent avoir une influence nocive sur la vision, mais c est la un probleme que les ingenieurs ont su resoudre en realisant de veritables circuits regulateurs a l interieur du vetement et de la capsule tant pour l oxygenation et l epuration de l air que pour sa temperature et son humidification

Mais les *facteurs psycho somatiques* semblent etre au moins aussi importants en ce qui concerne l environnement interieur

Des le moment ou l astronaute penetre dans la capsule il est isolé du monde exterieur Certes il demeurera en relation radio telephonique avec la terre durant la duree du vol mais l isolement et le confinement l attente d un depart dont on ne peut presumer la reussite constituent a n en pas douter une rude epreuve morale Je me souviens d avoir entendu Yaeger un des premiers pilotes de l avion experimental X dire que le moment le plus penible etait celui ou enferme dans son avion fusee il attendait, inactif d etre largué du bombardier qui le transportait en altitude Or dans certains cas il s ecoula plusieurs heures entre l insertion de l astronaute dans la capsule et la mise a feu de la fusee porteuse L apprehension

Ce que l'on a appelé *l'environnement météorologique* a suscité de nombreuses recherches avant l'envoi du premier homme dans l'espace. En effet, si la composition de l'atmosphère au niveau de la mer est favorable à l'homme, car sa densité constitue un écran protecteur contre les radiations ionisantes et les *météorites*, plus on s'éloigne de la terre, plus le milieu environnant devient hostile.

En pratique, on sait que les radiations primaires composées de protons (79%), de particules alpha (20%), et de noyaux lourds (1%), traversant l'atmosphère à l'altitude de 60 à 70 000 pieds, transmettent leur énergie aux *composantes* de cette atmosphère en produisant des radiations secondaires, *qui*, peu à peu, se transforment en chaleur. *Les effets nocifs des radiations* primaires augmenteront avec l'altitude, les noyaux les plus lourds apparaissant surtout au-dessus de 60 000 pieds. *Leur influence sur l'organisme*, et principalement sur les organes visuels ne parait pas devoir entraîner de troubles graves car il a été calculé qu'un pilote volant pendant 30 ans à une altitude de 75 000 *pieds ne serait exposé* qu'à une quantité totale de 108 r E M (Roentgen équivalent man). Enfin, les auteurs soviétiques n'auraient constaté *qu'un taux de 10 millirad* à *l'intérieur* des vaisseaux cosmiques et les animaux *placés dans les fusées* expérimentales n'auraient pas présenté *de modifications* biologiques importantes.

L'intégrité fonctionnelle du véhicule et les systèmes de protection prévus mettent pratiquement l'astronaute à l'abri des éventuels effets *nocifs des radiations* ionisantes, tout au moins pour les altitudes atteintes jusqu'à ce jour.

2 L'ENVIRONNEMENT INTÉRIEUR

Isolé dans une étroite capsule, couché sur un siège moulé d'après son corps, emprisonné dans un vêtement pressurisé truffé *d'électrodes*, la tête enfermée dans un scaphandre, l'astronaute se voit transféré dans un véritable "no man's land" où il va se trouver en présence de responsabilités que tous les entraînements antérieurs risquent de n'avoir pas toujours établi de façon précise.

Cet environnement intérieur comporte donc des facteurs physico-physiologiques et psycho-somatiques susceptibles de retentir sur sa vision.

Parmi les premiers, *l'oxygénation* joue un rôle important, car il n'est pas besoin de rappeler les effets de l'anoxie sur la perception visuelle. Une oxygénation de 100% est réalisée depuis la fermeture de la capsule au début du count down et durant tout le vol. Ce n'est que lorsque l'altitude de 25 000 pieds est atteinte lors de la descente que l'ouverture de valves permet l'entrée de l'air dans la cabine étanche. Une analyse de l'air de la capsule après une d'oxygénation à 100% a montré qu'il existait un taux de 90% d'oxygène.

Le maintien d'une *pression* correcte à l'intérieur de la cabine et du vêtement est également très important pour le bon fonctionnement de toutes les fonctions sensorielles. Le taux de pression de la cabine

et du vetement qui est d environ 14,7 livres par square inch lors du lancement passe a 5,7 apres une minute et demie et est maintenu à ce taux pendant toute la duree du vol jusqu'à une reprise de la pressurisation a 25 000 pieds lors de la descente apres ouverture des parachutes

La temperature a l interieur de la cabine et du vetement doit etre egalement maintenue a des taux permettant un bon equilibre physiologique Elle varie d environ 15 lors du depart et de la descente et aurait ete maintenue entre 14 et 24° C (58 F et 76° F) pendant toute la duree des vols de Nikolaiev et Popovich Glenn cependant se plaignit d une transpiration abondante durant les dernières phases de sa descente et de sa recuperation

L humidification de l air dans la capsule joue un role aussi important que la temperature etant donne les relations qui existent entre ces deux elements C est ainsi que l addition d une humidité de 10% a une temperature seche de 70 F fait passer cette derniere a 63 F et qu une humidite de 70% produit pour la meme temperature seche de 70 F un abaissement a 67 F Les experiences preliminaires aux divers vols spatiaux avaient montre que la temperature ne devait pas depasser 90 a 95 F (32 à 35 C) pour permettre l exécution normale des diverses taches incombant à l astronaute

Le souci d eviter les erreurs que pourraient provoquer des perturbations oculo motrices du fait des accelerations ou de l a pesanteur a fait repartir les multiples *cadrans et instruments de bord*, de façon à reduire l amplitude des mouvements oculaires du pilote L analyse du film de Shepard avait en effet montre qu etant donne la frequence du regard entre l indicateur de G et celui de carburant il etait indispensable de reduire la distance separant ces deux cadrans

Les gaz nocifs depuis l oxyde de carbone jusqu aux fumees et vapeurs irritantes, peuvent avoir une influence nocive sur la vision, mais c est la un probleme que les ingenieurs ont su resoudre en realisant de veritables circuits regulateurs à l intérieur du vetement et de la capsule tant pour l oxygenation et l epuration de l air que pour sa temperature et son humidification

Mais les *facteurs psycho somatiques* semblent etre au moins aussi importants en ce qui concerne l environnement intérieur

Dès le moment ou l astronaute penetre dans la capsule, il est isolé du monde exterieur Certes il demeurera en relation radio telephonique avec la terre durant la duree du vol mais l isolement et le confinement l attente d un depart dont on ne peut presumer la reussite constituent a n en pas douter une rude epreuve morale Je me souviens d avoir entendu Yaeger un des premiers pilotes de l avion experimental X dire que le moment le plus penible etait celui ou enferme dans son avion fusee il attendait inactif d etre largué du bombardier qui le transportait en altitude Or, dans certains cas il s ecoula plusieurs heures entre l insertion de l astronaute dans la capsule et la mise à feu de la fusee porteuse L appréhension

l'anxiete, si l'on ne veut pas parler de la peur, cependant bien naturelle en de telles circonstances, ont sur les processus mentaux superieurs, et par voie de consequence sur la vision, une influence non negligeable

Si les pilotes de jets ressentent parfois, a tres haute altitude, le "*break off*" prejudiciable a l'integrite visuelle, l'astronaute doit se trouver encore plus separe de la terre qu'il n'apercevra par instants, que sous l'apparence d'un fragment de mappemonde Heureusement, la multiplicite de ses taches ne lui laissent pas le temps d'epiloguer sur sa situation pour le moins anormale La surveillance des instruments, la frequence des indications qu'il doit transmettre au sol l'obligent a une attention soutenue Mais l'homme ne peut travailler intensement de façon continue que pendant des périodes relativement courtes s'il ne veut pas etre enclin a l'erreur et devenir inapte a remplir sa mission C'est la raison pour laquella, lors des vols sovietiques de longue duree, les astronautes durent consacrer au sommeil une partie de leur temps (8 heures sur 25 dans le cas de Titov)

Le vol spatial demande donc de l'adresse, de l'intelligence et un remarquable "self control" L'environnement exterieur et interieur qui situe l'astronaute en un milieu nouveau auquel son corps n'est pas adapte, l'expose a une succession de stresses susceptibles d'alterer le bon fonctionnement de ses fonctions sensorielles et de ses processus mentaux En effet, la capacite du systeme nerveux central d'interpreter et de realiser l'information transmise par les recepteurs sensoriels demeure a la base de l'efficacite humaine, et, en depit de toutes les experiences effectuees en laboratoire pour determiner, au point de vue visuel, le temps requis par la perception, l'integration, la decision et la reaction en connection avec les problemes particuliers survenant au cours de tels vols, il etait permis de supposer que les chocs physiologiques et les emotions etaient susceptibles d'aggraver *l'anisochronie* psychosensorielle

Il semble bien qu'il n'en ait rien ete

L'entrainement a certainement joue un role capital en mettant artificiellement le futur astronaute dans des conditions très proches de celles auxquelles il allait etre soumis en vol, et en lui apprenant ce qu'il devait regarder et ce qu'il devait executer en toutes circonstances La selection et un entrainement intensif, joints a la perfection des installations techniques ont donc permis aux diverses astronautes d'effectuer sans retentissement prejudiciable à leurs fonctions visuelles les vols spatiaux realises jusqu'a ce jour Et si leurs experience sont prouve l'efficacite de cette indoctrination prealable, elles ont aussi demontre l'aptitude, assez inattendue, de l'organisme *humain* a s'adapter a des conditions de vie totalement differentes de celles pour lesquelles il a ete conçu

LE CHAMP VISUEL EN ALTITUDE

A DUBOIS — POULSEN
Paris France

Les observations faites sur le champ visuel au cours des vols astronautiques sont actuellement gardees secretes aussi ne peut il etre question de se reporter à une etude bibliographique L experimentation etant d autre part inaccessible, il n est pas possible de donner la moindre precision dans ce domaine Notre propos sera plus modeste et nous nous contenterons de rapporter ce que nous connaissons des vols a haute altitude a la lumière de la litterature et des experiences que nous avons pu effectuer Les modifications du champ presentent non seulement un interet pratique qui pourra sans doute etre applique aux vols cosmiques mais aussi un intéret physiologique

Les variations constatees proviennent de l anoxemie des changements de pression des accelerations parfois d autres causes comme l eblouissement du aux modifications de l ambiance lumineuse Les plus connues sont celles qui sont dues a l anoxemie et aux pressions car elles peuvent etre facilement etudiées en caisson

I — DEPRESSION ANOXEMIE —

Il y a lieu d etudier successivement les modifications du champ visuel peripherique et celles du champ moyen, surtout dans la region de la tache de Mariotte on peut en principe opposer l extreme resistance des isoptères normaux du champ en altitude a l extra ordinaire labilite des caractéri tiques physiologiques de la region pericaecale

Les avis des auteurs different quant aux consequences de l altitude sur les limites peripheriques du champ visuel

En 1918 WILMER et BERENS sur 20 sujets soumis au caisson constataient entre 1600 metres et 3200 metres un elargissement passager et peu important des formes et des couleurs A 4800 m se produisait une contracton peripherique A 6000 m la contraction devenait plus importante et plus nette a la partie inferieure du champ et avait une amplitude de 7 environ Mais la technique n etait pas precise du point de vue photometrique

GOLDMANN et SHUBERT ont fait des experiences en caisson ainsi que dans des melanges gazeux pauvres en oxygene Le test etait un objet noir sur fond blanc Ils ont observe une contraction de la partie nasale et superieure du champ visuel vers 4200 metres Elle etait de 15 a l altitude de 6500 a 7000 mètres les limites temporales etant peu modifiees L inhalation d oxygène ramene le champ a ses limites Les auteurs pensent que l action est retinienne

FURUYA, sur six sujets, constate à 5000 mètres une contraction débutant du côté temporal, accentuée par la prolongation du séjour en altitude.

LIVINGSTONE avec le périmètre de CARGILL, en utilisant un test de 2 millimètres de diamètre trouve une contraction du champ pour des altitudes de 4500 à 5800 mètres. Elles sont symétriques et suivies parfois d'une tendance à l'élargissement lorsque le séjour en altitude se prolonge. Au delà de 10000 mètres, apparaissent des modifications plus nettes attribuées à l'aéroembolisme. Nous en reparlerons plus loin.

KYRIELEIS et SEIGERT ont repris les expériences de GOLDMANN et SHUBERT avec des tests blancs sur fond gris foncé. Même à des altitudes supérieures à 7000 mètres, ils n'ont pas trouvé de variations dignes d'être retenues. Elles seraient en effet de l'ordre de 1° à 3°, mais en réalité, leur technique est différente de celle de GOLDMANN. Ils font remarquer qu'il existe une considérable diminution de l'attention en altitude.

Pour MAC FARLAND, ces résultats contradictoires sont dus aux différences des techniques et surtout d'éclairement des tests. Il est bien certain que l'on ne peut guère confronter des expériences menées d'une manière aussi diverse, mais les erreurs proviennent surtout, selon nous, de la méconnaissance des fluctuations statistiques normales des limites périmétriques. D'expériences faites en périmétrie cinétique sur l'appareil de GOLDMANN modifié, et muni de dispositifs électroniques, nous avons pu conclure que les réponses présentent au sol une dispersion assez considérable. A la périphérie vers 60°, leur moyenne est de 5°. A la partie centrale, vers 10°, elles peuvent atteindre 10°.

Nous avons sur 15 sujets repris ces expériences en caisson, avec un périmètre de GOLDMANN, après mensuration du diamètre pupillaire qui ne varie d'ailleurs pas du fait de l'altitude. Le tracé normal des isoptères par la technique habituelle avec plusieurs combinaisons de surface et d'intensité pour le même isoptère, ne nous a montré aucune différence significative entre le sol, les altitudes de 3500, 4000 6000 et 7000 mètres. Nous avons alors recherché systématiquement le lieu de perception d'un test donné présenté dans le champ, en allant de la périphérie vers le centre, et nous avons répété l'expérience dix fois pour dessiner le nuage des points obtenus. Au sol la dispersion est de 5° dans le méridien oblique nasal supérieur avec le test de 5/4 à 50°, à 4500 mètres le nuage de dispersion reste le même. L'inhalation d'O_2 ne modifie rien. Avec un test de 3/3 sur le même méridien la dispersion est de 8° entre 30° et 38°, l'altitude de 4500 mètres ou l'inhalation d'O_2 ne changent rien. Il est certain que le fait de ne pas tenir compte de ces dispersions et de leur absence de variation peut faire croire à des différences d'une expérience à l'autre. On peut donc conclure que les isoptères restent remarquablement fixes dans les conditions normales d'altitude. Au delà, l'aéroembolisme modifie considérablement les choses (Fig. 2).

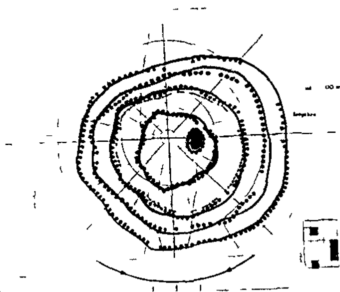


Fig 1
Isoptères du champ visuel à l altitude de 3700 m — En traits pleins isoptères au sol — En pointillé isoptères en altitude

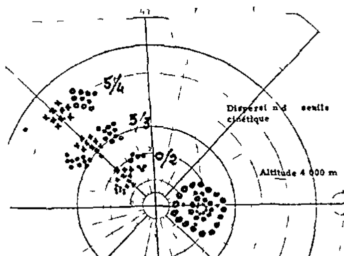


Fig 2
Dispersion de dix réponses avec les tests 5/4 3/3 et 0/2 Au sol croix — à l altitude de 4000 m cercles — en altitude sous 0² points noirs Les nuages de points restent les mêmes en vision peripherique Par contre autour de la tache de Mariotte ils s échelonnent concentriquement pour deux tests differents

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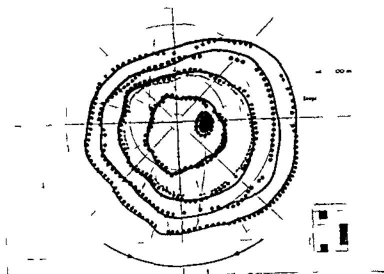


Fig 1
Isoptères du champ visuel à l altitude de 3200 m — En traits pleins isoptères au sol — En pointillé isoptères en altitude

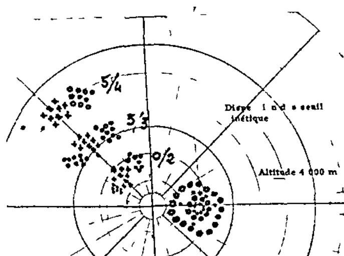


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a dépression et nous avons constaté que l'élargissement de la tache de Mariotte était constant en anoxémie et en dépression. Elle atteint des proportions importantes et si l'on mesure la tache avec l'index 3/3 de Goldmann sa surface peut doubler et même tripler. La grandeur de l'élargissement est une fonction non linéaire de l'altitude et de la vitesse d'ascension (lente dans nos expériences 10 m/sec).

L'élargissement est très intense de 2000 à 4000 m mais augmente moins au delà. L'inhalation d'oxygène diminue la grandeur de l'élargissement, ne ramène jamais la surface de la tache à sa valeur au sol, mais à une valeur intermédiaire. Ce fait est à rapprocher de ce que l'on sait du seuil du phénomène.

Nous avons en effet recherché ce seuil. L'élargissement commence dès les basses altitudes de 1000 ou 1500 mètres, à 2000 m, il est déjà très sensible et semble ne plus progresser que lentement à partir de 4800 mètres. A l'altitude de 1500 m l'inhalation d'oxygène reste sans effet sur l'élargissement pourtant déjà considérable de la tache. Il semble donc que le phénomène débute par un reflexe baropresseur sans doute auriculaire (Fig 3).

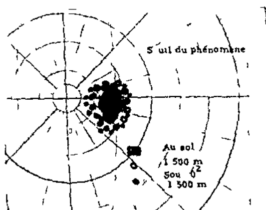


Fig 3
Seuil du phénomène d'élargissement de la tache de Mariotte. Les limites de la tache sont déjà plus grandes à *1500 m* mais l'action de l'oxygène est peu marquée.

De nombreux facteurs physiologiques sont en cause. Pour les analyser nous avons étudié l'influence de l'altitude sur le skiascotome. Celui-ci a été produit de deux *manières* différentes. La règle d'un double décimètre a été coincée horizontalement dans l'une des fentes de la coupole de l'appareil de Goldmann de manière à créer un obstacle sur le trajet des rayons du projecteur de tests. Elle portait donc une ombre sur les bords de laquelle apparaissait ou disparaissait le test suivant une loi complexe due à sa *forme* circulaire. La disparition se produit avec un retard vers l'intérieur de l'ombre, l'apparition avec un retard analogue en dehors de l'ombre. Les deux sens d'exploration

Ces expériences ont été néanmoins exécutées pour une seule *montée en caisson d'une matinée environ*. Les vols très prolongés ne sont pas inoffensifs surtout s'ils sont répétés au dessus du seuil normal d'adaptabilité soit 3,000 m -3,500 m. HALSTEADT a montré sur 20 sujets, les effets cumulatifs de l'anoxémie en les faisant séjourner 6 jours par semaine, pendant 4 à 6 semaines, 5 à 6 heures par jour *à 3000 mètres dans un caisson*. En réalité, les modifications du champ visuel ne purent être démontrées par les procédés classiques en attention concentrée, mais par celui *qui consiste à percevoir un test périphérique* alors que des couleurs et des formes sont projetées en vision centrale, c'est à dire en attention diffuse. Les modifications persistèrent au sol pendant plusieurs jours et pendant plusieurs semaines chez certains. Il s'agit en réalité beaucoup plus de troubles de l'attention dus à la fatigue, que de modifications proprement dites des seuils dans le champ visuel d'actions corticales que d'actions rétiniennes. On peut donc tenir pour certain que les seuils et leur graphique commode les isoptères, ne varient pratiquement pas pendant le séjour en altitude.

Il n'en est plus ainsi si l'on considère le scotome physiologique situé dans le champ visuel moyen que constitue la tache de Mariotte. *Ses variations sont connues depuis longtemps, GOLDMANN et* SHUBERT avaient déjà décrit son élargissement en altitude pour des tests blancs ou colorés. BATTENKO et BELOSTOTSKY, sur 15 sujets, ont fait la même constatation à 5000 mètres. La tache pouvait atteindre jusqu'à 271% de sa superficie normale au sol. L'élargissement disparaissait sous l'influence de l'oxygène.

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GENERAL CONCEPTS OF EALES S DISEASE

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Eales s (1880) (1) described the clinical syndrome of periphlebitis associated with recurrent vitreous haemorrhage in young individuals The syndrome is characterised by the presence of perivascular exudates with massive haemorrhages along one or more of the retinal veins and into the vitreous Haemorrhages in the vitreous ultimately result in the formation of glial bands projecting into the vitreous and ending into a traction detachment of retina

The aetiology of the disease is unknown and more often than not it is considered to be tubercular (2-8) or tuberculo allergic in origin (9 15)

We investigated a series of 50 cases of Eales s disease for Mantoux s reaction Our results reveal that only 16 of the 50 cases show tuberculin sensitivity in titres of 1/10,000 or over and in only 2 cases this reaction was positive in a titre of 1/100 000 The results are in no way different from a similar number of normal cases (Table 1)

Recent reports of fundus changes in sickle cell disease and abnormal haemoglobin conditions have focussed our attention to this aspect of pathogenesis of the disease (16 19)

Our cases were studied for the presence of any evidence of sickling red blood cells or abnormal haemoglobin We employed the technique of depriving the RBC of oxygen for the detection of the presence of sickle cells Electrophoretic method with veranol solution as buffer at PH 8 6 wa used for determining the abnormal haemoglobins The electrophoretic pattern of the haemoglobin of our cases did not differ from the haemoglobin of normal individuals The lack of sickling of RBC and the normal electrophoretic patterns, of haemoglobin (Figs 1 to 4) in cases of Eales s disease allows us to conclude that though vitreal and retinal haemorrhages are seen in sickle cell disease yet the two diseases are unrelated and sicklaemia has no aetiological bearing on Eales's disease

We also investigated the cases of this series for any evidence of macroglobulinaemia by the electrophoretic method and dilution plasma method but no evidence of macroglobulinaemia was found (Fig 5)

a depression et nous avons constate que l elargissement de la tache de Mariotte etait constant en anoxemie et en depression *Elle atteint* des proportions importantes et si l on mesure la tache avec l index 3/3 de Goldmann sa surface peut doubler et meme tripler La grandeur de l elargissement est une fonction *non lineaire de l altitude et de la* vite se d ascension (lente dans nos experiences 10 m/sec)

L elargissement est tres intense de 2000 a 4000 m mais augmente moins au dela L inhalation d oxygene diminue la grandeur de l elargissement, ne ramene jamais la surface de la tache a sa valeur au sol mais a une valeur intermediaire Ce fait est a rapprocher de ce que l on sait du seuil du phenomene

Nous avons en effet recherche ce seuil L elargissement commence des les basses altitudes de 1000 ou 1500 metres, a 2000 m il est deja tres sensible et semble ne plus progresser que lentement a partir de 4800 metres A l altitude de 1500 m , l inhalation d oxygene reste sans effet sur l elargissement pourtant deja considerable de la tache Il semble donc que le phenomene debute par un reflexe baropresseur sans doute auriculaire (Fig 3)

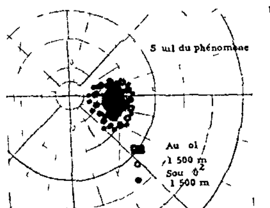


Fig 3
Seuil du phenomène d elargissement de la tache de Mariotte Les limites de la tache sont déjà plus grandes à 1500 m mais l action de l oxygène est peu marquee

De nombreux facteurs physiologiques sont en cause Pour les analyser nous avons etudie l influence de l altitude *sur le* skiascotome Celui ci a été produit de deux manieres differentes La regle d un double decimetre a ete coincee horizontalement dans l une des fentes de la coupole de l appareil de Goldmann de maniere a creer un obstacle sur le trajet des rayons du projecteur de tests Elle portait donc une ombre sur les bords de laquelle apparaissait ou disparaissait le test suivant une loi complexe due a sa forme circulaire La disparition se produit avec un retard vers l interieur de l ombre l apparition avec un retard analogue en dehors de l ombre Les deux sens d exploration

Ces expériences ont été néanmoins exécutées pour une seule montée en caisson d'une matinée environ. Les vols très prolongés ne sont pas innoffensifs surtout s'ils sont répétés au dessus du seuil normal d'adaptabilité soit 3,000 m–3,500 m. HALSTEADT a montré sur 20 sujets, les effets cumulatifs de l'anoxémie en les faisant séjourner 6 jours par semaine, pendant 4 à 6 semaines, 5 à 6 heures par jour à 3000 mètres dans un caisson. En réalité, les modifications du champ visuel ne purent être démontrées par les procédés classiques en attention concentrée, mais par celui qui consiste à percevoir un test périphérique alors que des couleurs et des formes sont projetées en vision centrale, c'est-à dire en attention diffusée. Les modifications persistèrent au sol pendant plusieurs jours et pendant plusieurs semaines chez certains. Il s'agit en réalité beaucoup plus de troubles de l'attention dus à la fatigue, que de modifications proprement dites des seuils dans le champ visuel d'actions corticales que d'actions rétiniennes. On peut donc tenir pour certain que les seuils et leur graphique commode les isoptères, ne varient pratiquement pas pendant le séjour en altitude.

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Une deuxième série d'expériences a été faite avec deux lames de polaroïd orientées à 90° l'une de l'autre. L'une était suspendue dans la coupole sur le trajet des rayons du projecteur, l'autre était montée sur l'objectif de projection lui-même. Lorsque les rayons polarisés du projecteur rencontraient le disque de polaroïd suspendu, la lumière s'éteignait. On obtenait ainsi un skiascotome plus maniable que le précédent car la variation des axes de polarisation permettait de ne pas supprimer complètement la lumière et de lui donner seulement des valeurs infraliminaires pendant la traversée du skiascotome. Les expériences ont été faites à 15° sur le méridien nasal horizontal. L'altitude et l'oxygène n'ont eu aucune influence (Fig. 6).

Ces constatations permettent une interprétation. Le skiascotome qui crée un ombre artificielle et de dimensions fixes sur la rétine, ne varie pas. L'angioscotome tributaire des vaisseaux varie. Le phénomène est donc vraisemblablement dû à la circulation rétinienne. La fixité des isoptères et du skiascotome exprime par contre les propriétés de résistance du tissu nerveux lui-même aux conséquences de la pression et de l'anoxémie. D'autre part, le seuil incroyablement bas du phénomène d'élargissement de la tache de Mariotte, le peu d'effet de l'oxygène à ces basses altitudes permet de penser que l'explication ne réside pas uniquement dans l'anoxémie. Un réflexe baro-presseur auriculo-oculaire doit aussi être en cause. On sait en effet les rapports de la physiologie auriculaire avec celle de l'angioscotome.

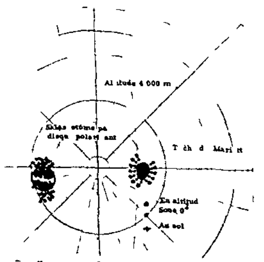


Fig. 6

Skiascotome analysé par un système de polarisation. Les points obtenus en pénétrant dans l'ombre ou en en sortant sont mélangés qu'ils correspondent au sol, à l'altitude de 4000 m ou à l'inhalation d'oxygène. Autour de la tache de Mariotte ils s'étagent concentriquement.

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Fig. 4

Mesures faites [illegible] par un bâton [illegible] des rayons lumineux [illegible] jusqu'à l'altitude de 4000 m.

Fig. 5

Mesures faites au sol, à 4000 m et sous O_2 à 4000 m. Les points représentant les [illegible] en [illegible] l'ombre [illegible] à 4000 m et sous oxygène [illegible] de la tache de Mariotte [illegible] correspondent à l'altitude de 4000 m [illegible] à la même altitude sous O_2.

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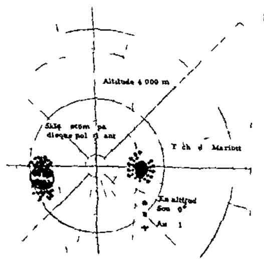


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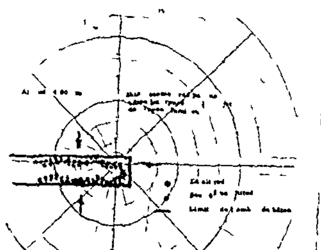


FIG 4
Skiascotome créé par un bâton interposé sur le trajet des rayons lumineux du projecteur périmétrique à l'altitude de 4000 m

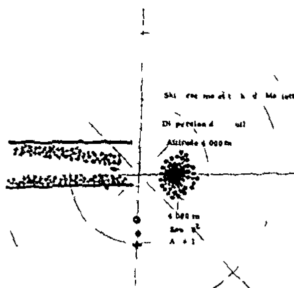


FIG 5
Skiascotome au sol, à 4000 m et sous O^2 à 4000 m Les points représentant les endroits où le test pénétrant dans l'ombre du bâton cesse d'être perçue sont mélangés au sol à 4000 m et sous oxygène Autour de la tache de Mariotte, ils s'étagent au contraire concentriquement Les plus externes correspondent à l'altitude de 4000 m, les moyens sont obtenus à la même altitude sous O^2

periphériques se rétrécissent Mais ces phénomènes sont très individuels et l on peut classer les sujets en tolérants et intolérants à l altitude *L anoxémie* fait apparaître dans le champ des flocons nuageux gris rougeâtres qui se déplacent en vagues successives du centre vers la périphérie Les nuages deviennent de plus en plus apparents au fur et à mesure que l anoxémie s accentue L inhalation d oxygène fait apparaître une lueur bleue intense, parfois verdâtre au niveau du point de fixation Le déplacement des nuages devient plus rapide puis ils disparaissent et les objets peuvent à nouveau être identifiés Les seuils absolus paraissent plus élevés en anoxémie quoique les processus d adaptation ne soient pas troublés d après LIVINGSTONE Nous n avons pas d expérience personnelle sur ce sujet

II ACCELERATIONS —

Les modifications de la pression et de l oxygénation ne sont pas les seuls facteurs de perturbation du champ visuel au cours du vol Les accélérations ou les décélérations entraînent des variations considérables qui peuvent aller jusqu à la perte totale de la vision Les accélérations angulaires étaient redoutées en aviation classique surtout lors des piqués, mais les rectilignes prennent une grande importance du fait de l emploi des fusées destinées à échapper à l attraction terrestre (Stewart Franks Kerr et Rose Ruff et Strughold, Marshall, Diringshofen Andrina) Un voile gris apparaît en général pour des accélérations tête siège à partir de 4G Si le pilote maintient cette valeur d accélération trop longtemps ou voisine 5G le voile noir apparaît rapidement Il débute du côté nasal et masque bientôt tout le champ visuel. Un degré de plus et le pilote perd conscience Peu de documents précis ont été donnés sur ce phénomène Des lampes colorées ont été placées dans le champ visuel du pilote La disparition des lampes périphériques l avertit de la perte du champ surtout nasal et commande de desserrer le virage Les temps nécessaires à la perte de la perception des lampes successives suivant les accélérations sont les seules données connues actuellement, la morphologie des champs n ayant pas été étudiée à notre connaissance ou n ayant pas fait l objet de publications Le *voile noir* est attribué à la fuite du sang vers les territoires veineux des membres inférieurs créant une anémie cérébrale L ischémie rétinienne serait aidée par la pression oculaire d après Diringshofen et d après Andrina d où l apparition du voile noir avant la perte de conscience Mais l ischémie carotidienne doit diminuer cette pression, facteur dont n ont pas tenu compte les auteurs Oh je pose aussi la question de savoir pourquoi dans ces conditions la compression oculaire permettrait une résistance accrue aux accélérations? Seule la connaissance des champs visuels permettra de trancher le débat et de savoir si l origine du phénomène est cérébrale ou rétinienne

Les accélérations siège tête sont plus rares Elles élèvent la pression dans les vaisseaux cérébro-rétiniens à — 2 G elles créent avec la céphalée des scotomes négatifs dont la forme la surface et la position sont mal connues Elles donnent surtout lieu au voile rouge

Ces conclusions sont en désaccord partiel avec des expériences faites par BIETTI Cet auteur a constaté que l'inhalation d'oxygène rétrécit les angioscotomes normaux et ceux de *plusieurs maladies*, surtout du glaucome Cependant, dans 20% *des cas, l'angioscotome pourrait s'élargir, ce qui expliquerait les effets constatés par* DUGUET et J P BAILLIART, complètement opposés à ceux de ROSENTHAL Le skiascotome, pour BIETTI, rétrécirait par contre constamment sous l'influence de l'oxygène, ce qui indiquerait une amélioration de la fonction rétinienne, se traduisant par une disparition plus lente et une apparition plus rapide du test Le résultat sur *l'angioscotome* de l'oxygène ou de sa privation serait expliqué par le jeu des facteurs qui agissent sur son étendue Calibre vasculaire, grandeur du *flux* sanguin, sensibilité rétinienne En général, la privation d'oxygène diminue la sensibilité rétinienne en même temps qu'elle crée la vasodilatation L'angioscotome et la tache de Mariotte s'élargissent, ce qui est en accord avec les données de la majorité des auteurs Mais *chez certains sujets, le calibre des vaisseaux diminuerait et l'angiosco*tome serait plus étroit malgré la diminution de la sensibilité rétinienne

Les modifications de calibre des vaisseaux pourraient donc être variables suivant les sujets, mais le skiascotome varierait toujours dans le même sens et serait ainsi plus fidèle que l'angioscotome Nous *n'avons pas retrouvé cette variation du skiascotome* Là aussi, la dispersion statistique des réponses est considérable au niveau de ses bords, et il est nécessaire d'en tenir compte, conformément à ce que nous avons dit plus haut pour la mesure des isoptères

Il résulte néanmoins des études des auteurs et de nos propres *expériences que dans les effets de l'anoxémie* et de la dépression, se mêlent les modifications vasculaires rétiniennes et les troubles de la sensibilité du tissu nerveux proprement dit

Ce qui précède concerne les dépressions relativement lentes de l'ordre de 10 m sec Les décompressions brusques sont différentes *dans leurs effets Elles provoquent* l'apparition d'altérations du champ visuel périphérique avec contractions irrégulières du champ que la montée lente vers l'altitude ne peut produire *D'après* WHITTER, il y aurait aussi des scotomes bilatéraux et homonymes se déplaçant par un mouvement centrifuge vers la périphérie du champ visuel Ils s'effacent rapidement en 10 à 16 minutes après le retour au sol La région maculaire n'est jamais intéressée et les dimensions de la *tache aveugle ne seraient pas* modifiées LIVINGSTONE constate aussi des scotomes multiples avec contraction périphérique des champs Ces manifestations coïncident *souvent* avec un syndrome migraineux classique, accompagné de céphalées et de tendances syncopales On les interprète souvent comme des conséquences de *l'aeroembolisme* dans les artérioles terminales et de spasmes surajoutés

Le champ visuel nocturne présente des modifications assez *différentes* de celles du champ photopique D'après LIVINGSTONE, le scotome maculaire nocturne normal s'élargit en même temps que la tache de Mariotte, qui réagit *comme en vision* diurne Les limites

produit pas dans la lecture des appareils de bord, l éblouissement est donc surtout périphérique et gêne alors la vision centrale

Il s apparente de loin et tout au moins en ce qui concerne l ambiance générale, a ce qui se produit lorsqu au laboratoire un sujet est soumis a une luminance de préadaptation puis plongé dans l obscurité Dans l aéronef, la deuxième ambiance reste lumineuse, mais il existe un passage où le seuils sont très fortement perturbés dans leur valeur et leur topographie et par conséquent inadéquats Nous ne connaissons pas de travaux précis sur cette question de l éblouissement général le sujet restant en lumière photopique ou mésopique les recherches actuelles portant surtout sur l éblouissement de la région centrale du champ visuel

De nombreuses recherches restent a faire sur le comportement du champ visuel en haute altitude et tout est loin d être dit sur ce sujet Les premières acquisitions sont cependant d un haut intérêt, a la fois pratique et théorique et suscitent des interprétations physiologiques difficiles

L expérimentation a été faite au centre physiologique de l armée de l Air Française qui a mis généreusement a notre disposition ses caissons a dépression Nous remercions tout particulièrement le Médecin Commandant Perdriel de l amabilité avec laquelle il s est constamment tenu a notre disposition

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dont l'interpretation est encore plus difficile que celle du voile noir En effet, la repletion excessive des vaisseaux retiniens en pathologie ne donne pas la sensation de rouge

On sait que des etudes tres poussees ont ete faites, grace a des machines centrifugeuses pour tenter d'eviter les phenomenes de voile noir et de voile rouge et d'augmenter la resistance aux accelerations La position couchee diminue le gradient de pesanteur tete tronc, on resiste donc mieux dans cette position aux accelerations Mais deux positions sont possibles, l'accelerations se produisant dans le sens face anterieure, face posterieure du thorax, ou " eyeballs in " comme disent les auteurs anglais, ou dans le sens face posterieure, face anterieure " eyeballs out " Cette derniere position serait la meilleure, mais provoquerait un flot de larmes tres genant pour le pilote Les positions couchees, sur le cote sont prejudiciables au fonctionnement cardiaque

On admet en general qu'un pilote en position ordinaire sur son siege sans protection speciale, peut supporter 5 G d'acceleration et — 3 G dans l'autre sens, une combinaison elastique reduisant les deplacements sanguins augmente la tolérance a 6 G La tolérance aux accélerations en ligne droite, qui est le cas des fusees, serait plus forte, 8 G avec eyeballs in, et plus de 8 G avec eyeballs out Mais le flot de larmes se produit comme nous venons de le dire On envisagerait meme d'immerger entierement le corps du pilote dans une cuve remplie d'eau L'accroissement d'inertie du corps serait alors contre balance par l'inertie de l'eau La tolerance pourrait monter a 32 G, pendant 5 secondes

Les consequences de l'etat d'apesanteur sur l'oeil sont mal connues Les equipes sovietiques n'ont rien rapporte sur ce sujet La centrifugeuse est ici inutilisable et seul un parcours parabolique rigoureusement controle en avion peut produire cet etat pendant une fraction tres courte de temps Il semble que rien ne se produise du point de vue visuel, mais on ne sait pas si la prolongation de cette situation ne pourrait pas retentir sur l'oeil par un mecanisme indirect de modifications hydriques vasculaires et de regulation nerveuse

Quoiqu'il en soit, l'etude des phénomenes oculaires dus a l'acceleration a surtout porte sur leurs conditions d apparition plus que sur l'analyse méthodique de leurs modalites et de leur mecanisme intime

III EBLOUISSEMENT

Restent enfin les phenomènes d'eblouissement qui proviennent de la modification de l ambiance lumineuse et qui peuvent perturber grandement le champ visuel Le ciel est assombri en haute altitude mais les objets eclaires par les rayons solaires deviennent tres brillants Les nuages, les plans metalliques reflechissent violemment la lumiere Les post images sont très intenses, persistant longtemps de 2 a 3 minutes Toutes les varietes d'eblouissement peuvent se voir, peripherique ou central Celui ci n'est pas le plus frequent puisque le pilotage a ces altitudes n'est plus une question de visibilite exterieure Il ne se

AETIOLOGY

Being unable to find any evidence of other disease to account for the haemorrhage he was inclined to attribute the syndrome to a disturbance of autonomic control "affecting both the circulatory organs and the digestive system leading on the one hand to partial inhibition of the muscular movements of the bowels and to vaso motor contraction of the vessels of the alimentary canal with inhibition of its secretory functions and on the other hand to compensatory dilatation of the systemic capillaries especially those of the head, and in these cases of the retina causing over distention of the venous system with liability to rupture on the occurrence of any intensifying cause" He considered this an explanation of the headache, epistaxis, retinal haemorrhages and the tortuosity and fullness of the retinal vessels and temporal artery

TREATMENT

Having tried various remedies he concluded that there was no evidence of their doing much good and contented himself with symptomatic treatment It will be interesting to learn what progress has been gained in our knowledge of the aetiology and treatment of this condition *in the 80 years since* the time of Eales's description and if any further information has been obtained on the part played, if any, by the autonomic nervous system in this condition

produit pas dans la lecture des appareils de bord l eblouissement est donc surtout peripherique et gene alors la vision centrale

Il s apparente de loin, et tout au moins en ce qui concerne l ambiance generale a ce qui se produit lorsqu au laboratoire un sujet est soumis a une luminance de preadaptation puis plonge dans l obscurite Dans l aeronef la deuxieme ambiance reste lumineuse, mais il existe un passage ou les seuils sont tres fortement perturbes dans leur valeur et leur topographie et par consequent inadequats Nous ne connaissons pas de travaux precis sur cette question de l ebbuissement general le sujet restant en lumiere photopique ou mesopique les recherches actuelles portant surtout sur l eblouissement de la region centrale du champ visuel

De nombreuses recherches restent a faire sur le comportement du champ visuel en haute altitude et tout est loin d etre dit sur ce sujet Les premieres acquisitions sont cependant d un haut interet, a la fois pratique et théorique et suscitent des interpretations physiologiques difficiles

L experimentation a ete faite au centre physiologique de l'armee de l Air Française qui a mis genereusement a notre disposition ses caissons a dépression Nous remercion tout particulierement le Medecin Commandant Perdriel de l amabilite avec laquelle il s est constamment tenu a notre disposition

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ASPECTS CLINIQUES DE L ANOXIE EN OPHTALMOLOGIE AERONAUTIQUE

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Malgre les progrès realises par l Aeronautique moderne, et l emploi de moyens permettant de maintenir un apport suffisant d oxygene aux sujets se trouvant meme aux altitudes les plus elevees le problème de l anoxie reste actuel en medicine aeronautique et spatiale

Parmi les manifestations de l anoxie, celles relatives a l organe visuel occupent une place importante Depuis de nombreuses annees elles ont intéressé me collaborateurs et moi meme et je me rapporterai principalement a no etudes au cours de cet expose

Nous pouvons etudier les modifications provoquees par l anoxie avec avant tout les moyens utilisés dans la physiologie aeronautique, qui permettent de reproduire à terre les conditions d hypoxie Nou voulons parler de l emploi des chambres à depression de l inhalation de melanges gaseux pauvres en oxygene et de la methode de reréspiration

Des resultats superposables peuvent etre obtenus en ce qui concerne l exploration de certaines fonctions oculaires par la com pression dynamometrique du globe oculaire qui entraine une ischemie locale Celà permet de mettre en evidence que l action du deficit en oxygene sur certaines fonctions (sens lumineux acuite visuelle centrale et périphérique dimensions des scotomes physiologiques sens chroma tique fréquence critique de fusion etc ,) est en grande partie expliquée par des phénomenes au niveau de la retine

L anoxie entraine au niveau de l appareil visuel des alterations de type *sensitivo sensoriel* des *alterations circulatoires* des *troubles de la motilite oculaire intrinseque et extrinseque* et enfin des *modifications de la transparence des milieux* oculaires

En ce qui concerne les *modifications sensitivo sensorielles*, je rappelerai que le deficit en oxygène a seulement une action modeste sur *l acuite visuelle centrale* [2 47-52] sauf *en* vision à basse illumination ou la diminution de l acuite visuelle est plus *nette* [53] elle a une action similaire sur le *pouvoir de resolution* de la retine [14] Les phenomenes sont évidents seulement a haute altitude

Les *limites* peripheriques du *champ visuel* ne sont que peu modifies [20-24-26 57] mais on signale parfois de scotomes Les scotomes

physiologiques rencontres chez les sujets normaux subissent des modifications plus importantes On observe en general un elargissement de la tache aveugle (3-22-7) sous effet de l'anoxie, accompagne par un elargissement des angioscotomes (50-51-7) qui en partent Dans un certain nombre de cas, au contraire, on observe un phenomene oppose, c'est a dire leur diminution (40-7) Il faut interpreter ces differences comme etant en rapport avec un comportement different du calibre vasculaire selon les sujets L'exploration de la sensibilite retinienne par un moyen plus precis, c'est a dire la determination du scotome artificiel de Goldmann ou "skiascotome" par la methode de la "tache d'huile", met en evidence une augmentation costante de ce scotome sous l'effet de l anoxie, (7) cela revele une diminution de la sensibilite retinienne

L'acuite visuelle stereoscopique est peu influencee par l anoxie a altitudes moyennes, alors qu il y a accentuation des troubles à des altitudes superieures (16) (6-8,000 m) La dimension des images retiniennes (iseikonie) (44) n'est pas modifiee par le deficit en oxygène

Les *sens lumineux* (21-23-29-33-34-35-36-37) est tres sensible a l'anoxie Ces alterations se relevent deja a des altitudes moyennes (2 500 m) et augmentent avec l altitude On a interprete ce phenomene de differentes façons, (43) en l'attribuant a des modifications du metabolisme des substances photochimiques retiniennes, et de la position du pigment retinien, a des troubles de la circulation, mais surtout à une action directe sur les elements nerveux, qui se sont releves comme ayant particulierement besoin d'oxygene a l'obscurite

Le *sens chromatique* n est pas fortement influence par le deficit en oxygene, mais si l'on emploie des techniques d'examen precises, il y est toutefois sensible L anomaloscope permet ainsi de constater l'apparition de legeres protanomalies ou deuteranomalies, (17) ainsi que l augmentation de l'amplitude de deplacement de la vis, lors de la determination de l'equation de Rayleigh On constate une aggravation des troubles chez les sujets ayant deja un ses chromatique defectueux Le test de Farnsworth indique egalement des anomalies, et en particulier l'apparition d'une tritanomalie (18) L'anoxie entraine, de plus, lorsqu elle est elevee, des alterations de la efficience chromatique dans le bleu, dans le vert et dans le jaune au " color aptitude test " (52)

L'anoxie a de plus la caracteristique de reduire la *frequence critique de fusion* (10) des stimulus lumineux repetes, surtout au niveau de la partie centrale de la retine, mais aussi, lorsque l'anoxie est elevee, de la portion peripherique l ischemie du globe oculaire entraine des resultats analogues

L'examen en anoxie des deux indices d'excitabilite retinienne et plus precisement de la *rheobase* et de la *chronaxie optiques*, a mis en evidence une diminution de l excitabilite de ces deux indices deja a des altitudes peu importantes (2 000 m), en particulier en ce qui concerne la chronaxie (50a)

l' activité électrique de la retine (*electroretinogramme*) est aussi altere par le deficit en oxygène La composante negative de l ERG (onde a) serait, selon certains auteurs (15) plus resistante a l anoxie que l onde positive b et l'onde x ceci surtout chez le chat mais aussi chez l homme (19) lorsque l anoxie est elevée Nous avons au contraire personellement trouve une diminution de l onde a sans changements du trace (1)

D autres observations traduisent les variations du comportement du *reflèxe oculo cardiaque* (48) (augmentation du seuil avec sensibilite moindre lors du deficit en oxygene) et de la *sensibilite corneenne* (augmentee dans l anoxie aussi bien aigue (32) que chronique) (57) L anoxie influe de plus sur les phenomènes de *rivalite retinienne*, (46) augmentant de façon toutefois legère, l inhibition

Rappelons enfin, l influence sur les *phenomenes endoptiques* se revelant par l apparition spontanée de phosphènes et la diminution de la visibilite des houppes de Haidinger Le comportement des images posthumes (25 39) est interessant il y a une augmentation de la periode de latence qui est inversement proportionnelle à l import ance du stimulus qui entraine leur apparition, et une prolongation de leur duree cela explique certains phenomènes d eblouissement constates aux hautes altitudes par ex lors du vol au dessus des couches compactes des nuages refletant fortement la lumiere (55)

Quant aux *altérations circulatoires* (40) dues a l anoxie notons avant tout l augmentation de la pression arterielle retinienne (11) dans la majorite des cas (75%) avec acceleration de la circulation retinienne, diminution du calibre vasculaire, augmentation du tonus des vaisseaux coloration violacée des artères à l ophtalmoscope Dans l anoxie chronique des alterations plus graves de la rétine apparaissent hemorragies et oedemes (54)

La *pression oculaire* est aussi influencee, mais de façon legere On observe une faible elevation lors de l anoxie aigue (11) et dans la décompression et une faible diminution dans celle chronique (30) La *perméabilite de la barrière hemato ophtalmique* est augmentee (28 29a, 29b)

L anoxie entraîne des modifications importantes au niveau de la *musculature oculaire intrinsèque et extrinsèque*

On observe l apparition d une legere exophtalmie (56) par hyperexcitabilite sympathique lors de l anoxie chronique avec de plus des alterations de la *motilite pupillaire* (13) et de *l accomodation*, ainsi que de la musculature extrinsèque du globe oculaire

Les pupilles en effet se dilatent et le myosis provoque par l illumi nation est plus bref et moins prononce Cependant la vitesse de contraction et de decontraction pupillaire augmente L effet de restitution obtenu par les stimulus acoustiques sur la pupille est moindre ou meme absent quand l anoxie est grave et le stimulus lumineux faible la pupille peut meme devenir tout a fait inexcitable Signalons un phenomène singulier l apparition d anisocorie statique

physiologiques rencontres chez les sujets normaux subissent des modifications plus importantes On observe en general un elargissement de la tache aveugle (3-22-7) sous effet de l'anoxie, accompagne par un elargissement des angioscotomes (50-51-7) qui en partent Dans un certain nombre de cas, au contraire, on observe un phenomene oppose, c'est à dire leur diminution (10-7) Il faut interpreter ces differences comme etant en rapport avec un comportement different du calibre vasculaire selon les sujets L'exploration de la sensibilite retinienne par un moyen plus precis, c'est a dire la détermination du scotome artificiel de Goldmann ou "skiascotome" par la methode de la "tache d'huile", met en evidence une augmentation costante de ce scotome sous l effet de l'anoxie, (7) cela revele une diminution de la sensibilite retinienne

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gueries *declanchement* ou aggravation *d un nystagmus latent L'administration d oxygene* inhale a la pression atmospherique exerce au contraire une action opposée, qu on peut utiliser dans des buts therapeutiques, meme si ses effets sont transitoires

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ou dynamique, ou bien la disparition d'inégalités pré-existantes lors du déficit en oxygène.

En ce qui concerne l'accomodation, on note chez les presbyopes, au début un éloignement majeur du punctum proximum, mais aussi, chez les sujets jeunes, une augmentation du temps d'accomodation et de la fatigue accomodative. Ce phénomène est beaucoup plus accentué dans la vision binoculaire que dans celle monoculaire, en raison évidemment, de la plus grande sensibilité des muscles striés de la convergence, les muscles lisses du corps ciliaire étant moins sensibles. En effet, la convergence est facilement fatiguable dans l'anoxie alors que le punctum remotum de la convergence s'éloigne.

On observe encore d'autres troubles de la musculature oculaire (8) lors de l'anoxie, en général on constate une tendence à l'ésophorie dans la vision éloignée (qui peut réduire une exophorie pré-existante), une tendence au contraire pour l'exophorie dans la vision de près, et aussi l'apparition de déséquilibres verticaux, et, exceptionellement, de diplopie. L'alcool (8) potentialise les effets de l'anoxie, même modestes. Le pouvoir de fusion (9) est réduit en anoxie, surtout en adduction, l'amplitude de fusion est au contraire mieux conservée, si l'anoxie n'est pas très grave.

Elle détermine aussi des troubles des mouvements oculaires associées, comme par ex. ceux de la lecture (12). On constate une augmentation du temps employé pour lire un texte, un ralentissement des mouvements oculaires, une augmentation des erreurs avec mouvements de retour, une augmentation du nombre des fixations des groupes de lettres, une plus grande fréquence du clignement.

Dans le groupe des altérations de la motilité oculaire, signalons enfin les modifications provoquées par l'anoxie sur le nystagmus opto-cinétique, (47) dont la fréquence est réduite alors que l'on observe une légère augmentation de l'amplitude des secousses.

Je rappellerai enfin que l'anoxie provoque *d'étranges altérations de transparence* des milieux oculaires. En dehors des troubles superficielles transitoires de la cornée, provoqués par l'emploi prolongé des verres de contact (qui entraînent une sorte d'asphyxie), ou par le séjour dans une atmosphère d'azote, nous signalons surtout ici les opacifications du cristallin, que l'anoxie grave et l'asphyxie provoquent chez le rat (4, 5, 41, 42) et, de façon moindre, chez le lapin (41, 42) mais non chez l'homme, elles sont reversibles. Ces opacités peuvent être expliquées par une diminution de la pression osmotique de l'humeur aqueuse, une chute des chlorures, une augmentation de la production d'acide lactique.

En dehors des modifications que j'ai énumérées jusqu'ici et qui sont déterminées par l'anoxie chez les sujets ayant un appareil oculaire normal, je pense qu'il est intéressant de rappeler que lorsqu'il y a déjà des *altérations oculaires*, (6) celles-ci peuvent être *aggravées* par un déficit en oxygène: élargissement de scotomes de différentes origines (y compris ceux observés dans le strabisme en vision monoculaire et binoculaire), *réapparition d'une diplopie* lors de parésies apparemment

SPACE OPHTHALMOLOGY

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Aerospace ophthalmology is a continuing extension of aviation ophthalmology, a discipline that was created when aviation medicine developed into a well organized science during the early years of the twentieth century It is highly dependent upon the teachings and experience gained from clinical ophthalmology but possesses a number of distinct and unique features that set it apart

Historically the ophthalmologist has occupied a primary role in aviation medicine The acknowledged father of aviation medicine in America was an ophthalmologist, General Theodore C Lyster (2)

The first Aviation Medical Research Laboratory in the United States was established at Hazelhurst Field, in Mineola, Long Island, in 1918 Its director was an ophthalmologist, Colonel William H Wilmer and the Chief of the Ophthalmology Department was Dr Conrad Berens Outstanding basic work performed at this laboratory developed many of our present concepts Studies dealing principally with the effects of oxygen lack upon visual acuity, accommodation, convergence and retinal sensitivity led Drs Berens and Wilmer to conclude that the visual symptoms taking place during decompression, or at altitude were due to lack of oxygen and not to the reduction of barometric pressure as had been claimed by some authors (19)

A perusal of aviation medicine literature discloses many other well known contributors in the field of ophthalmology that I am unable to credit at more length in this paper Many of the problems that we now face in aerospace flight are not entirely new and the research performed by early workers has contributed significantly to our present successes in space flight

Since man s creation he has reached out to conquer new frontiers with unshakable faith and has turned his dreams into reality Throughout the ages man has felt the compelling attraction of the stars and planets longing for the day when he might experience the fascination of flight into space This era was ushered in with startling abruptness on October 4 1957 when the Soviet Union orbited the unmanned artificial earth satellite Sputnik I Within a few months this was followed by Sputnik II containing the first space dog and then by the United States satellite Explorer I These rapidly occurring successes in space exploration made the peoples of the world suddenly realize that the age of manned space flight was rapidly approaching

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Eales s disease has also been ascribed to the hormonal disorders like hypopituitarism[20 23] and relative deficiency of androgens We have not done any hormonal assays but therapy with androgens has given equivocal results suggesting indirectly that deficiency of androgens is probably not a causative factor

Deficient oxygen carrying capacity of the blood may affect the capillary walls of the retinal blood vessels leading to retinal and vitreal haemorrhages We estimated the oxygen concentration by Van Slyke s method in 50 normal individuals and 50 cases of Eales's disease of the same age group Our observations do reveal that in a majority of cases of Eales s disease the oxygen concentration of the blood was subnormal (Table II) This deficiency probably leads to venospasms oedema or retina increase in fragility of small capillaries and greater permeability of venules and exudation

The aetiology of Eales's disease is as yet uncertain and remains conjectural Deficient oxygen carrying capacity without sickling of R B C is an important finding and the factors producing this deficiency of oxygenation require further experimentation

CLINICAL PICTURE

The disease is conventionally described to be present in apparently healthy young males In this series only two cases were seen in females and the rest were males The minimum age in this series was 18 years and the maximum age was 45 years Those in the later age group came in 4th or 5th attack The average age of the onset of the disease has been 23 years

Eales had pointed out that in most of the cases the L L is affected earlier than the right eye and this observation is fully supported by our series as in 32 of the 50 cases either the left eye was the only involved eye or it was affected earlier than the right eye

The patient complains of a sudden painless blurring of vision on awakening in the morning The degree of blurring depends on the extent of haemorrhage and the vision may even be reduced to perception of light One eye is involved earlier than the other but eventually both eyes are affected The ophthalmoscopic picture depends upon the severity of the haemorrhage If there is massive haemorrhage in the vitreous fundus reflex is absent but a black or faint red reflex may be seen If the haemorrhage is minute and the patient complains of only few black spots in the visual field the vitreous may look clear and haemorrhages can be seen in the retina Intermediate grades of haemorrhages in the vitreous may be visible The vessels of the retina especially the veins are tortuous The haemorrhages are usually seen in the periphery near or over the veins They may rarely be found around the disc and macular area is hardly ever involved The haemorrhages are large and of varied shapes and their origin from the involved veins can be made out, though the veins are temporarily obscured by the haemorrhages Around the veins marked perivascular

mile altitude range there are alternate periods of 45 minutes of day light, 45 minutes of night, and the pupils often will be dilated for brief exposures to sunlight

Illumination from the sun is approximately 10 000 foot candles (108,000 lux) at the earth s surface at noon in summer in middle latitudes (11) At altitudes above the atmosphere, the illumination is increased approximately 30 per cent to about 13 600 foot candles (146,800 lux) (9) We find that the irradiance in space is increased over that at sea level in about the same proportion as the solar constant going from 1 4 at sea level to 2 cal /cm ^{2}/min ^{1} above the atmosphere an increase of approximately 50 per cent This may then result in a tendency to subjective underestimation of the retinal burn danger (13) since the sun s irradiance would increase 50 per cent while the subjective brightness rises only 30 per cent At sea level the critical time of exposure to obtain a foveal burn has variously been estimated as about one minute or less (5) In space it may result in 10 to 15 seconds in an unprotected normal eye (4 16)

Within our own solar system the irradiance of the sun s image on the retina is independent of the distance due to the focusing power of the eye Although the size of the image changes inversely with distance the amount of energy reaching a unit area in unit time is not decreased since there is no attenuating atmosphere present Therefore even though the image size decreases with distance the critical time of exposure may remain nearly the same

In most situations retinal burns do not present as serious a possi bility as the transient reduction in retinal sensitivity which follows illumination at high levels (3) If reduced sensitivity results in a pilot being unable to perform critical visual tasks promptly, the results could prove fatal The literature is filled with data on dark adaptation but most of it is not relevant to the problem of flash blindness There has been little work done to determine the sensitivity changes within the first few critical seconds or fractions of a second Recently investigators have undertaken this task (3 10 12, 14) This information is vital and is sorely needed for guidance in the development of protective devices

Numerous protective devices from fixed filters to self attenuating variable density photoreactive filters have been proposed Of these, the phototropic filters are the most fascinating and should they become perfected they could be utilized to great advantage in the windows of space vehicles and helmet visors of the astronauts A dependable solution is necessary not only for comfort but as a means of protection to the astronaut For example, orbital rendezvous will require intricate maneuvers and dazzle from a sudden reflection or direct visualization of the bright solar disc during final closure could be disastrous

It has been suggested that judgment of distance in space may be somewhat more difficult since some of our clues such as aerial

The year 1961 brought the pioneer orbital flights of the Russian Cosmonauts Gagarin and Titov and the suborbital flights of American Astronauts Shepard and Grissom. The year 1962, highlighted by the successful orbital flights of Glenn and Carpenter, from the United States, and the dual orbiting of Popovich and Nickolayev, from the Soviet Union, firmly established this new era of "man in space."

We, as doctors, can feel a sense of pride in the participation of medicine along with our allied sciences in helping to make this great adventure possible. Most of us are familiar with the problems of atmospheric flight and the great strides investigators have made in meeting these challenges. Most of these problems are still with us, and now with space flight new problems appear and the old ones become more complex.

Let us briefly consider this hostile environment the astronaut encounters by reviewing the various altitudes at which man requires support equipment. The visual system is particularly sensitive to oxygen lack. At only 5,000 ft. (1.5 km.) the first indication of decreased oxygen is manifested by diminished visual acuity at night. The symptoms of hypoxia become increasingly evident above 10,000 ft. (3 km.) with the corresponding decrease in partial pressure of oxygen. At 16,000 ft. (4.8 km.) there is a 10 per cent loss in night vision ability, and from this altitude up to 25,000 ft. (7.5 km.) accommodation, convergence power and fusional amplitude continue to decrease. Above 25,000 ft. (7.5 km.), without support, both vision and consciousness are lost and permanent brain and retinal damage can occur. At 50,000 ft. (15 km.) the time of useful consciousness without proper protection is 8 to 15 seconds or the time required for blood to go from the lungs to the brain. Above 63,000 ft. (20 km.) often referred to as the Armstrong line, the barometric pressure has dropped to 47 mm. Hg, a point which is the same as the water vapor pressure of body fluids, and boiling of body fluids occurs (1). At 80,000 ft. (25 km.) conventional pressurized cabins are no longer effective. Beyond 140,000 ft. (42 km.) there is no protective umbrella against the ultraviolet rays of solar radiation. Above 100 miles (160 km.) sound disappears as the strange darkness of space is reached and heat transfer by conduction and convection is lost (17).

Space environment does not become apparent at any one altitude, and the gradual change is visual as well as physical. As the astronaut proceeds into space, his surroundings appear totally different. The sky above becomes a deeper blue as the atmosphere begins to thin, and with an absence of a light absorbing and light scattering medium, the overhead sky becomes completely black except for the stars. The moon and the stars appear brighter and the stars no longer twinkle (16).

Although the human eye is amazingly adaptable and performs effectively over a range of illumination of greater than 100 million to one, it does not adjust instantly. Strughold and Ritter point out that the problem of glare is more serious in space flight because of the relatively short day-night cycle (15). In vehicles orbiting in the 100–500

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concern from galactic radiation solar flares and trapped radiation as found in the Van Allen belt Since these cannot all be shielded out reasonably one must attempt to predict within limits their effect on space cabin occupants Therefore, a combined study by the Department of Bionucleonics and the Department of Ophthalmology, at the USAF School of Aerospace Medicine, has been undertaken This study has utilized the synchrocyclotron at the University of California Berkley and other sources to determine the immediate and long term effects on the eye (6) The main purpose of these studies is to determine the relative biological effectiveness (RBE) of these high energy ionizing radiations

In addition to the problems of actual space flight aerospace ophthalmology has the challenge to perform basic investigations utilizing a unique population that is relatively asymptomatic and apparently healthy Most of our past medical knowledge is derived from patients studied in clinics and hospitals who are ill or presumed to be ill Thus they constitute a pre selected group and do not provide an adequate basis for studying the natural history of many diseases nor do they provide the basis of normality Long range studies of flying personnel can provide this information In the field of ophthalmology much valuable information can be obtained by the establishment of a tonographic repository as we have planned at the USAF School of Aerospace Medicine

Using present and future astronauts as excellent laboratory specimens about which we have an incredible amount of data we as flight surgeons, can develop information to the benefit of the practicing ophthalmologist and Mr and Mrs average citizen

Dr David Cogan in his editorial in the May issue of the Archives of Ophthalmology pointed out ophthalmology s expanding interest in an expanding universe The vistas of aerospace ophthalmology are exciting ones The role of the ophthalmologist in space medicine is evident and the need for his talents will continue

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perspective which is due to atmospheric attenuation, will not be present Glenn accurately estimated the distance of the Atlas missile from his spacecraft for short distances, as proven by an analysis of the trajectory data (8) Thus, we feel that at least for close distances accurate estimations can be made by experienced pilots This can prove particularly important in final closing maneuvers to achieve rendezvous

Space myopia, or empty field myopia, has been considered by some authors to be a potentially serious problem (7, 18) Many investigations have been undertaken on this problem, and I am sure many more will be performed To date, there has been no direct evidence of difficulty by any of our pilots in orbital missions *

All flyers and most researchers in aviation are familiar with the problem of increased "G" forces or gravitational stress which can result in dimness of vision and blackout This problem is well understood and well investigated, however, the problem of weightlessness was novel to all and as a result a number of controversial predictions have been made When the astronaut encounters prolonged weightlessness, he finds an entirely new experience, and his eyes take on an added importance Under gravity free conditions the mechanoreceptors, such as the otolith organ, the pressoreceptors of the skin, etc , do not function, and the eye is the only sense organ he can rely upon for orientation (16) Many researchers feared that the eye would not be capable of normal function in a zero gravity condition Some hypothesized that the extraocular and ciliary muscles could be affected and result in alterations of muscle balance, accommodation, and fusion The short periods of weightlessness of less than one minute that could be achieved in parabolic flight did not offer enough information to support or refute these speculations Debriefing reports from the successful flights of Glenn and Carpenter indicate that there is no apparent difficulty and support the reliability of the eye in space flight Astronaut Glenn, in his reports, stated ' Maintaining orientation was no problem, but I believe that the pilot automatically relies much more completely on vision in space than he does in an airplane where gravity cues are available '(8)

In space we are exposed to the whole range of the electromagnetic radiation spectrum of the sun, from x rays of about 10 angstroms in wavelength to radio waves up to about 10 meters in wavelength The whole range of cosmic ray particles in their original primary form and the energy with which they enter our solar system are encountered (17) Most ophthalmologists are familiar with the effects of ultraviolet rays, visible rays, infra red rays, and lower energy x rays With increased interest in space we now become concerned with the effects of high energy proton and, to a lesser extent, alpha radiations which make up the majority of the radiation of biologic

* Personal communications

VISUAL PERCEPTION OF MOVEMENT

by

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What appears to be the fundamental factor in the visual perception of movement of an object against a featureless background is the comparison of sensations of eye movement and the sensations of movement produced by an image travelling across the retina Thus the visual perception of movement can be determined by the movement of an image across the retinal mosaic but one must take into account also movement of the eyes for if one is tracking a moving object the image may be stationary upon the retina yet there is a sensation of movement because the eyes are changing position To this sensation of movement is of course added the retinal sensation of movement produced by the relative displacement of the background in the opposite direction to that of the moving target Thus if one is looking at a moving target against an untextured or otherwise empty visual field the threshold for movement perception is higher than that in which one observes a target against a textured background

The different patterns of eye movements have now to be considered First the fast phase Usually eye movements made in the course of search or in looking from one object to another consist of saccades of very high velocity (about 600 /sec according to Westheimer) and these are interspersed with fixational pauses During the fast saccade there is no visual perception of any detail whatsoever under normal circumstances The question of whether there is in fact during this saccade any retinal or central inhibition appears to have been solved by some recent experiments carried out at Farnborough in which we have shown that an electronic flash of some 10 microseconds duration can be seen during the fast phase of eye movement In this experiment the flash was triggered off by the corneal retinal potentials so that one could cause the flash to appear either at the beginning towards the middle or towards the end of the saccade On all occasions the flash was seen Nor could it be suggested that what was detected was the visual after image for if this had been the case the position of the flash would have been displaced so that it appeared in line with the final fixation point There was in fact displacement which one could attribute to the inevitable delays in the retinal processes but the

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illusion on the basis of the system diagram shown in Figure 1 This figure shows primary efferent activity arising from such factors as labyrinthine activity and giving rise to a sensation of movement as well as to an actual contraction of what we have called the "agonist" extra ocular muscles When the subject who fixates a small light source perceives as a result of the small retinal displacement that his fixation has drifted to one side, there is initiated a fixation reflex to centralise the fixation spot again This fixation reflex calls for a pattern of efferent activity again but aimed at the extra ocular muscles whose action is

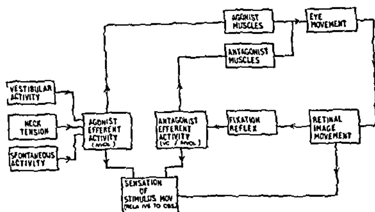


FIG 1 (Whiteside 1963)

antagonist to the involuntarly acting group This efferent activity pattern also gives rise to a sensation of movement and it seems that this is the sensation which dominates possibly because the pattern of efferent activity is one resulting in small saccadic corrections *rather* than slow drifts and therefore having a character of bursts or volleys rather than slower changes in the frequency of the efferent volley It is evident that in this figure the antagonist efferent activity and the associated circuit constitutes virtually a servo loop which *can open* simply by removing the visual stimulus and therefore the information from the mis alignment detector

Similarly it is probable that the eye movements in the *oculogravic* illusion give rise to a sensation of movement of the visual field *upwards* with increase in g The fact that eye movement is not usually *detected* in observations on the oculogravic illusion may thus be due to the presence of a fixation point and therefore to *the fact that the* servo-loop is closed If the loop is opened the character of the eye movements as a result of increase in acceleration becomes more obvious It consists most frequently of a downward movement with increase in g or an upward movement with a decrease *in* g

displacements caused by these delays indicated that the flash was still being seen during the first phase of the eye movement.

If there is no appreciable inhibitory change one must conclude that the visual scene is not impressed upon the retina simply because the eye is moving too quickly. Further experiments carried out with a mirror rotating at such a speed as to cause a visual scene to move at 600°/sec likewise prevented the subject from seeing any detail whatsoever, although he was, of course, able to detect an electronic flash of very short duration. There was on this occasion no apparent displacement of the flash since no eye movement was involved and therefore since there was no temporal difference in the appreciation of the retinal stimulus and of the simultaneous eye position. The experiments in which such a difference was found suggest that the retinal image takes longer to be perceived than does the information on eye position.

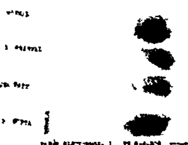
Thus, normally, the individual sees the visual world in a series of fixational pauses during which fixed objects about him give rise to fixed images upon the retina and therefore to no movement. On such a basis it seems unnecessary to invoke more complex explanations to account for the stability of the visual world. During such fixational pauses, of course, an object moving across the visual field will give rise to an image tracked across the retina and therefore to a visual sensation of movement.

Although in scanning there are normally (in general) no eye movements sufficiently slow to enable one to see the external world during that eye movement, there are slow eye movements which occur either during the tracking of a moving object or which occur reflexly for example from labyrinthine activity. Furthermore it has been shown by Ditchburn and Ginsborg that if the eye is in darkness and at rest, it undergoes a series of slow drifts of fairly large magnitude in spite of the fact that the subject is attempting to maintain his gaze in a constant direction.

It has been suggested, that the sensation of position of the eye is associated with the size of the efferent volley (Merton 1961). Thus if the eye is displaced passively, a visual after image impressed upon the retina will seem to remain perfectly stable in front of the subject whereas, of course, the external scene will appear to move since its image is moving across the retina. On the other hand, if one makes or initiates an active eye movement, whether it be voluntary, or involuntary as a result of labyrinthine activity, a visual after image will be seen to move in the direction of the eye movement. A visual scene may appear to move in the opposite direction or to be spatially stabilised. However, if the external field of view consists only of a small light source observed in darkness, this too will appear to move but in a direction apparently opposite to that of the slow drift.

As a result of observations made in Pensacola, Florida, Graybiel and Niven and I have suggested an explanation for the autokinetic

Fig 1 Showing normal haemoglobin pattern in cases of Eales s disease



2 Showing normal haemoglobin pattern in cases of Eales s disease

Fig 3 Showing normal haemoglobin pattern in cases of Eales s disease

4 Showing normal haemoglobin pattern in cases of Eales s disease

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Such an upward movement has been demonstrated in experiments on what has been called the elevator illusion This refers to the apparent movement downwards of the walls of a lift when it is beginning its descent Figure 2 shows the pattern of eye movement occurring at the onset of such a deceleration It is evident that the eye moves upwards by some 5 in a short space of time It is probable that the

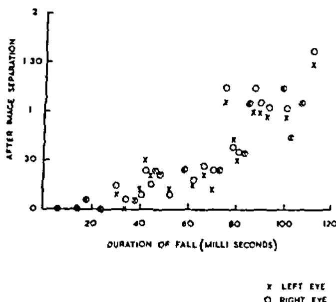


FIG 2 (Whiteside 1963) *

presence of this eye movement in response to a step change from one to zero g is due to the fact that there has been insufficient time for servo loop to correct a fast change in the agonist activity

To resume, it seems therefore, that we observe the visual world in a series of fixational pauses and that during these pauses any image moving on the retina is interpreted as moving We may, however have a slow eye movement occurring reflexly, in which case, a comparison of the rates of movement of the eye and of a retinal image likewise provides information as to visual movement relative to the observer The presence of a pattern of efferent activity which is attempting to move the eyes may also give rise to sensation of movement when the image on the retina is fixed, as when one is observing a visual after image, or a scene which is stabilised on the retina This sensation of movement which may arise in paralysis of extra ocular muscles due to organic or experimental causes such as the effect of curare gives rise to apparent drifts of the visual scene in the same direction as that of the attempted eye movement It seems possible that such an explanation could be extended to take account of many other neurological conditions in which illusory drifts of the visual scene are observed

decreased Foveal threshold was tripled(7) Brown and Burke showed that visual reaction time is increased by acceleration(8)

Dazzling or glare may occur while traveling into the sun or above a surface which has a high reflectance such as clouds snow, or desert It may produce functional disturbance such as the loss of adaptation when a night pilot is exposed to intense searchlight beams Experimental studies of high intensity carbon arc flashes of only 0 1 second duration have shown recovery sufficient to read aircraft instruments to be as long as three minutes(9) The symptoms due to prolonged glare are headache, ocular pain and concentric contraction of the visual field Older pilots are greater affected (10) Glare becomes of increasing importance the higher one ascends At altitude, the upper stratosphere becomes increasingly deep blue due to the decreased atmospheric scattering and the lower field becomes brighter with greater glare Strughold and Ritter(11) have pointed out that in the blackness of space an astronaut with dilated pupils may experience functionally disturbing glare when he looks into the brilliant disc of the sun

Infrared retinal burns may be suffered at altitude unless the pilot is alert to its hazards On earth Cordes found it required one minute exposure to sunlight to produce a retinal burn(12) In space it may be less then ten seconds High speed electromechanical goggles have been developed which close in less than 500 micro seconds after a high intensity flash such as a nuclear explosion

Ultraviolet Light those wave lengths shorter then 3 050 A units have poor penetration and seldom produce deep ocular damage Its ill effects may be manifested as snow blindness lid edema, superficial keratitis lens fluorescence unless obviated by special filters Most of the ultraviolet radiation is absorbed by water vapor and clouds of the lower atmosphere Consequently the higher one ascends the greater the possible effects of the ultraviolet light

Other high energy radiation in the form of alpha and proton particles may be encountered in cosmic rays and more intensely in the area of the Van Allen Belt In the dark adapted eye these may be experienced as slashes of light by the astronaut The highly sensitive epithelium of the lens capsule is easily damaged by radiation Culver and Newton have warned against flights of long duration through these high energy belts and especially during periods of Solar Activity (13)

Wind Blast Visual Problems only occur as accidents either from windshield breakage or canopy ejection or from pilot ejection from the cockpit of a high performance aircraft Wind tunnel experiments have shown facial tolerance to 300 m p h for 30 seconds without severe ocular damage Bail out survivors from military jet craft have endured greater wind blast stresses Goggles are unsatisfactory as at this speed they are torn off or broken Helmets or ejection capsules afford the best protection

DISCUSSION

PROBLEMS RAISED IN OPHTHALMOLOGY BY RECENT ADVANCES IN AVIATION

By

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The ophthalmologic problems associated with modern advancement in aviation *per se* differ only in degree with those so well presented at the Ophthalmological Society of Paris, by Mercier and Duguet seventeen years ago(1). The problems related to space travel offer some new difficulties. The Physio pathology of vision at altitude are largely those of anoxemia. Between 5–10,000 feet, the slightly reduced partial pressure of oxygen reduces the night vision of the unsupported subject. Psychomotor and sensory disturbances associated with altitude sickness may occur above 14,000 feet, Above 30,000 feet, unconsciousness and circulatory collapse will ensue. McFarland and Halperin have shown a shift of the retinal sensitivity curve with anoxemia which accounts for the gradual darkening and depression of the vision that fliers have experienced at high altitudes(2). The Stereoscopic sense and color vision are little affected by anoxemia, but there is reduction in accommodation(3). Motility, convergence, and oculomotor balance are adversely affected by lack of oxygen. Night vision as mentioned is greatly depressed by anoxia. Ocular tension even in the glaucomatous eye is not affected by oxygen deficiency or altitude.

Decompression effects are largely due to aero embolism which may manifest as migrainous scotomata or hazy vision. It has occurred in pilots flying at low altitude who have been previously scubadiving for recreation.

Visual troubles due to rectilinear or centrifugal forces are dependent on the posture of the subject. Nystagmus, ptosis, over convergence and grey out may develop if the subject is sitting and exposed to positive gravitational force(4). Blackout may occur after several seconds of + 4.5 G. While in the horizontal position the subject may be able to tolerate + 12 G for several minutes before blackout(5). The tolerance to negative gravitational forces is much less. Red out and retinal hemorrhages may occur after minus 3 G forces of short duration.

The effects of acceleration are similar to the centrifugal forces appreciated in a horizontal position, and ocular physiologic tolerances are high. At 4 G acceleration, White(6) found the visual acuity to be

Recent series of mid air collisions and near misses have resulted in a tremendous interest in collision avoidance measures To avoid collisions the following factors should be known to a pilot about the intruding aircraft 1 Presence and location 2 Identification 3 Heading 4 Distance or Range 5 Altitude 6 Speed 7 Attitude 8 Intended Maneuver Investigation is continually being made to determine if exterior lighting systems, smoke and vapor trails optical devices, or training procedures can augment any of these eight types of information Studies at the Applied Psychology Corporation at Arlington Virginia have shown that pilot subjects report most reliance on apparent relative motion of a target in making their judgements about the outcome of simulated collision problems(18)

1 Presence and Location Ignorance of the location of an intruding target will produce probable detection distance of only 1/4 or 1/3 of the threshold range During day the presence of an aircraft intruder may be accentuated by color schemes In general the under surfaces of a plane should be a very dark color The upper surfaces of the plane should be a very light hue with a high reflectance factor, and all colors sharply delineated If broad surfaces such as the rudder are used for displays of fluorescent paint the intruding craft will be more conspicuous under many conditions(17b) At night detection is increased by high intensity navigation lights Flashing helps but may be disorienting to both the pilot and observer The basic concept still is valid that any constant bearing observed between the intruding aircraft and a spot on the observers windshield will indicate the existence of the potential colli ion(17c)

2 The Identification of an Aircraft will give cues as to the possibility of collision The difference between a jet and a helicopter intruder will call for appropriate response

3 The Heading of the Intruding Aircraft should be as precisely determined as possible so that a pilot can check his own course and estimate the flight path of the intruding aircraft

4 Range and Distance At night estimation of range becomes a most difficult task Some cues exist in the intensity and pattern of running lights but since at present there is no standardization in aircraft navigational lights this becomes most difficult Aircraft bearing high intensity lights and quadrant identification signals are best detected

5 Relative Altitude In most cases pilots judge relative altitude with reference to the horizon This may be extremely difficult at night Signal light configuration indicating altitude has met with little success At higher altitudes estimation of the precise height of the intruding aircraft can be miscued by the attitude of the observers plane

6 Speed Speed may be estimated by the type of aircraft identified

7 Attitude An appraisal of the attitude of the intruding aircraft may quickly show that it is executing an avoidance maneuver, or rolling into a collision course

Vibration It has been shown that the visual acuity is impaired by large amplitude vibration Above 100 cps little change in vision was noted The maximum affect of vibration occurs generally in the 25 to 40 cps range, and again from the 60 to 90 cps(14) These frequencies are present in modern aircraft of the propeller variety, and especially in helicopters Vibrations of the aircraft, especially of the instrument panel produce ocular and general fatigue These vibrations can be dampened by proper seat and instrument mounting

Weightlessness There is some evidence of minimal loss of visual acuity associated with weightlessness Pigg and Kama(15), found that there was 6% loss of acuity at 0 gravity of a 14 seconds duration Orientation of a pilot in space craft will depend primarily on vision in the absence of reliable gravitational cues Illusions of object displacement occur in weightlessness due to oculogyric and oculogravic reflexes(16)

Visual Problems in Collision Avoidance The safe occupancy of airspace depends on the ability of each pilot to maintain vigilance and take corrective action when necessary All pilots are not of the high caliber and training as those who brought you to the meeting The activity of general aviation accounts for the greater part of flying in the United States General aviation covers all flying except that preformed by the public carriers, and the military, and accounts for more than three times the flying time of the air carriers in their domestic operations Over half of the landing and departures at the larger airports and virtually all the activity at the smaller airports can be attributed to general aviation(17) The proportion of pilots who possess the ability to fly a plane with sole reference to instruments is small The modernization of private aircraft places a single engine plane of 200 m p h at the command of pilots who may have minimal training and experience All pilots during VFR weather must maintain vigilance for their mutual safety Visual Flight Rules cover those flying conditions in which there is a visibility greater then one mile distance, and a cloud ceiling of over 1 200 feet The requirements for visual flying conditions about airports and in high traffic density areas and along air traffic routes is more critical Less than these conditions necessitates the filing of an instrument flight plan In this case separation of aircraft is the responsibility of air traffic control However, the pilot flying on an instrument flight plan during clear (VFR, or marginal weather) may be given a false sense of security that he alone is privileged to occupy that particular air space His vigilance may be somewhat dampened by the multitude of intra cockpit duties More then 85% of air collisions have occurred during VFR operations In 1960 there were 24 collisions in the United States of America In 1961 there were 22, and in the first nine months of 1962 there were 12 Many of these accidents can be attributed to inattentiveness Short has examined the difficulty of dividing a pilot's attention between cockpit and the exterior, in the search for intruder aircraft(17) Monitoring the cockpit reduces external vigilance in the order of 60%

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8 The Intended manuever of each aircraft remains the most difficult to estimate

In high traffic density areas one reasonable solution to collision danger is *en route* radar surveillance by air traffic control This has been instituted on the Eastern Seaboard of the United States Even with this help visualization through haze layers may be difficult Often in the usual haze over New York, with reported visibility of over five miles I fail to see the traffic that radar assures me is only two miles away Many pilots of far greater experience report the same difficulty

Two types of radar help exist Precision Radar systems provides exact 3 dimensional location of an aircraft as it approaches for a landing However, general radar surveillance can neither intrinsically identify a target nor show its altitude Transponders within the aircraft more frequently in the future will automatically couple this information into the radar screen below Four types of airborne anticollision devices based on radio, micro wave or infrared transmission have been studied by the government of the United States since 1958 Due to lack of promising developments this study is being discontinued (19) Thus the responsibility for collision avoidance during V F R conditions rest on the visual capabilities of the pilot Any ophthalmologist who treats even the occasional recreational pilot should bear this well in mind

Cockpit Visual Problems For many years men have been flying aircraft which have been designed by engineers who have given poor recognition to the visual problems of the pilot In most planes, and especially those in the air carrier classification there is restricted windshield visibility In many cases there is only a narrow view ahead, right and left, and seldom below and to the rear This is caused by the multitude of instruments and controls which need be placed within the pilots reach or view Windshield wipers in many cases are inadequate Reduction of visual acuity is partially due to the pre empting of accommodation by unclean windshields(20) Prolonged search into an empty field also produces a functional myopia Autokinetic illusions and vertigo trouble the untrained pilot (21)

Within the cockpit the pilot is dependent upon antiquated instrumentation which has been engineered on a Space Available basis This has resulted in a uniform three inch diameter instrument dial, each one of which presents a single bit of information to the pilot about the complex workings of his ship

The instruments are of stereotyped size, shape and scale, regard less of the function indicated and show many of the following faults

The instruments are poorly placed This introduces a high parallactic error of the needles in certain portions of the dial for those peripherally mounted

In one aircraft carrier, the needle and ball, a primary flight instrument is placed behind the control column so that if needed in an emergency it would be obscured

The presbyopic captain who must read the Doppler Scale mounted ten inches above his forehead next scan the brilliant horizon and then re adapt to read the dim radar scope on the cockpit floor, has his visual patience sorely tried

Poor grouping of instruments is noted especially in the light planes where instruments related to aircraft performance engine performance navigation and communication are scattered at random over the span of the panel

The lighting of an instrument may be inadequate or shadowed by exterior light

To preserve dark adaptation red light is used for panel illumination Pilots complain that the extensive use of red light diminishes its effectiveness as a warning signal

The warning flag indicating malfunction of a navigational device may be a small poorly illuminated red flag Many a well trained pilot has failed his flight check and been grounded for inattentiveness to this inadequate warning

Auditory aids in warning devices are being slowly developed The pilot must sample 20 or 30 odd bits of information from his instrument panel in order to determine the performance of his aircraft In the laboratory the best possible sampling rate that man can achieve probably is in the order of three instruments per second In the aircraft this speed is impossible Therefore scanning 20 or 30 instruments requires time Because of the lag inherent in each instrument the information is already an historic fact A delayed reaction period of 2 5 seconds ensues and then the pilot makes appropriate movement of his controls At this time he must predict the final readings of his instruments and take corrective action before his aircraft arrives at its intended situation If he does not he will have over controled his aircraft

Visual Problems of Landing The intra cockpit visual tasks of the pilot at take off and landing and at all times during visual flight conditions must be superseded by the exterior visual stimuli received by the pilot Thus even though he has monitored his cockpit instruments carefully on take off the pilot who is unaware of a flight of starlings rising from the runway ahead meets with disaster The need for instantaneous change from instrument to visual flight is apparent when we consider the pilot who approaches for landing at night with poor visibility He is relying completely on instruments until the time he reaches the middle marker of the instrument landing system where he is only several hundred feet above and ½ mile away from touch down He must quickly shift his gaze from the instruments to the runway This transition has often resulted in a misjudgement of the elevation of the runway even under the best of lighting conditions

Landing Systems To obviate these difficulties, work is progressing in two directions The British have developed an automatic landing system in which the pilot performs only a monotoring function to insure that the landing system is functioning correctly This system offers great promise It has been estimated that the margin of error, of malfunction of this device is in the order of one to 10 landings for this Triplex System(22) However, it will be many years before it could be possible to install such automatic systems in even the larger airports of the world In another direction there is work being done to reflect a simulated runway and instrumentation on a half mirrored surface directly on the windshield The pilot can control his plane by collimnated instrumentation and by the external visual cues which will appear as he lands This type of system promises to be less costly and be able to be used in remote and poorly equipped airports through out the world This method of interpretation of flight information would be the same in I F R flight as in V F R flight and transition error is virtually eliminated(23)

Considering the visual and other problems of the pilot in the atmos phere one may question whether man can efficiently safely control space craft Compared to automatic systems, the human pilot has a slow response, is subject to greater error and fatigue and requires food and sleep At the Institute of Aerospace Science Meeting in Seattle, the relative efficiency of man and machine were compared It was felt, largely, that the machine should be the performer and the role of man relegated to monitoring and decision making Robert Gilruth, Director of Manned Space Center of National Aeronautics and Space Adminis tration however, showed that considering weight, space, cost and reliability, a manned system would be superior to a fully automatic system

This return to manual control of flight is considered the greatest advance the Gemini and Apollo capsules will make over Mercury missions The successful piloted flights of Shirra in Sigma Seven and of the near rendezvous (6 3 miles) of Colonel Popovich and Major Nikolayev have ably demonstrated this capability

Once again the visual potentiality of man will be subject to the greatest test In all aeronautic endeavors the knowledge of man's physical limitations has served to stimulate engineering developments which have complimented his capabilities Thus the coordinated efforts of the Engineer the Pilot and the Physician can eventually surmount problems of modern aviation

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Eales s disease has also been ascribed to the hormonal disorders like hypopituitarism[20 23] and relative deficiency of androgens We have not done any hormonal assays but therapy with androgens has given equivocal results suggesting indirectly that deficiency of androgens is probably not a causative factor

Deficient oxygen carrying capacity of the blood may affect the capillary walls of the retinal blood vessels leading to retinal and vitreal haemorrhages We estimated the oxygen concentration by Van Slyke's method in 50 normal individuals and 50 cases of Eales s disease of the same age group Our ob ervations do reveal that in a majority of cases of Eales s disease the oxygen concentration of the blood was subnormal (Table II) This deficiency probably leads to venospasms oedema or retina, increase in fragility of small capillaries and greater permeability of venules and exudation

The aetiology of Eales s disease is as yet uncertain and remains conjectural Deficient oxygen carrying capacity without sickling of R B C is an important finding and the factors producing this deficiency of oxygenation require further experimentation

CLINICAL PICTURE

The disease is conventionally described to be present in apparently healthy young males In this series only two cases were seen in females and the rest were males The minimum age in this series was 18 years and the maximum age was 45 years Those in the later age group came in 4th or 5th attack The average age of the onset of the disease has been 23 years

Eales had pointed out that in most of the cases the L E is affected earlier than the right eye and this observation is fully supported by our series as in 32 of the 50 cases either the left eye was the only involved eye or it was affected earlier than the right eye

The patient complains of a sudden painless blurring of vision on awakening in the morning The degree of blurring depends on the extent of haemorrhage and the vision may even be reduced to perception of light One eye is involved earlier than the other but eventually both eyes are affected The ophthalmoscopic picture depends upon the severity of the haemorrhage If there is massive haemorrhage in the vitreous fundus reflex is absent but a black or faint red reflex may be seen If the haemorrhage is minute and the patient complains of only few black spots in the visual field, the vitreous may look clear and haemorrhages can be seen in the retina Intermediate grades of haemorrhages in the vitreous may be visible The vessels of the retina especially the veins are tortuous The haemorrhages are usually seen in the periphery near or over the veins They may rarely be found around the disc and macular area is hardly ever involved The haemorrhages are large and of varied shapes and their origin from the involved veins can be made out though the veins are temporarily obscured by the haemorrhages Around the veins marked perivascular

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roentgen equivalent, man (REM) It is the same with gamma rays, but the *relative biological effectiveness* (RBE) value is one It is the same with thermal neutrons as it is with gamma rays except that it is five REM and five RBE value Fast neutrons have a REM of ten, and RBE value of ten and protons have a REM of ten and RBE value of ten Alpha particles however, have twenty REM to a REP and twenty as the RBE value The establishment of permissible dose, permissible dosage rate and permissible amount of radioactive material deposited in the body is dependent on the results of biological investigations and past experience Sufficient experience has been accumulated with gamma rays and X rays up to about a million volts, so that the permissible dose and permissible dosage rate are quite definitely known In the case of radiations in space there has been much less experience Permissible amounts of radioactive material deposited in the body have not been exhaustively investigated for all radioactive isotopes Even in the case of X rays and gamma rays the long term genetic effects are not known with certainty There is good reason therefore to introduce liberal safety factors

The primary aim of all radiation protection procedures is to reduce radiation exposure to below permissible amounts Radiation hazards fall into two classifications (1) Those hazards in which there is a possibility of radioactive material entering the body and (2) those hazards in which there is a possibility of external radiation only

Electrical apparatus in which high voltages are employed is not considered a source of harmful radiation when in use However one should assume that such apparatus represents a potential hazard until it is established otherwise

With reference to alpha radiation except in the case of alpha particles from high energy accelerators there is no problem in protecting the eye from such particles originating outside the body since the energy from them is reduced to zero by a few centimeters of air or a few millimeters of solid material However since they are particularly hazardous inside the body it is necessary to use suitable equipment designed to evaluate the hazard due to contaminated air or surfaces

The problem of shielding the eye from external beta radiation is not formidable Reasonable thicknesses of solid material will obstruct all beta particles emitted from radioactive isotopes One should not overlook the fact however that secondary X rays are produced in the shielding material by the action of beta particles on matter Such X rays are more penetrating than primary beta particles and they become a significant safety hazard where high intensity beta sources are in use Therefore every installation should be checked with appropriate measuring equipment to determine the overall effectiveness of the shielding

Lucite or a similar plastic is a convenient transparent shielding material easily fabricated The thickness of air necessary to stop all beta particles of a given energy is of interest where unshielded beta sources are being handled The hazard occasioned by the introduction

OPHTHALMIC PROBLEMS IN AVIATION

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This discussion is limited to protective measures for the eye in space Nuclear emanations can produce harm from a distance All of the means of shielding the eye in space flight are considered The type of clothes, goggles, and other protective measures are related Biologically a sufficient quantity of radiation is the amount of energy that can be absorbed per gram per disintegration under a given set of conditions The radiation measuring instruments in use today depend on the ionizing properties of radiation for their operation Studies are now being carried out throughout the world to decontaminate persons exposed to sudden acute effects of radioisotopes The type and amount of medication to be used will be based on monitoring of areas The first of these medications will be in the form of excretory stimulants, later drugs will be developed to change the chemistry of gamma emitting substances

We know now that man can travel a few hundred miles from the earth and stay a few days in space Although a short period of weightlessness has no deleterious effects on the eye we are not certain about effects of a longer period We can expect deterioration of the optic nerve, retina, and extra ocular muscles If man moves out further he will have to protect the eyes from effects of corpuscular radiation Perhaps some device will be developed which can be included in a space capsule that will counteract weightlessness

Light clothing is known to absorb less heat than dark clothing Goggles should be leaded and darkened, leaded and protective aprons should be worn

Biologically, the significant quantity of radiation is the amount of energy that can be absorbed per gram per disintegration under a given set of conditions The radiation measuring instruments in use today depend on the ionizing properties of radiation for their operation The more common are the ionization chamber, the proportional counter, and the Geiger Mueller counter In all three types of detectors, the essential features are two electrodes across which an electric field is applied in an appropriate gas or mixture of gases A typical instrument consists of two oppositely charged electrodes placed in an ionization chamber Chambers should be air wall equivalent

Reports of dosimeter readings provide a basis for estimating exposure and for adjusting plans accordingly The readings indicate when exposure or re exposure should be avoided, and thus can also be used as a basis for controlling the exposure of the eye

One roentgen of X rays equals one *roentgen equivalent, physical* (of energy absorbed) (REP), the amount of biological damage is one

The concept of radiation injury is not new Sunlight is an example Man has known about the effects of sunlight for a long time He has known about the effects of fire There are sensory warnings for light and fire There is however no sensory warning for gamma radiation Man made detecting devices must be used to help in this problem Radiation damage is not immediate as it is with fire or sunlight

Nuclear emanations can produce harm from a distance Germs cannot do that They must enter the body Sunlight may cause harm from a distance but its effects at the time that it is being received is known to the senses The characteristics of radiation hazards are the following Lack of perception by the senses a delayed effect, and ability to penetrate thick solid material The permissible dose of radiation is the main criterion in the measurement of safety and there are three factors over which one has control These are distance time and shielding Distance follows the law of the inverse square Time has maximum safe time as the basis and shielding attenuates the radioactive power of a substance To understand the hazards of radiation the constituents of matter must be understood

From the standpoint of the biological effect of neutrons upon the eye two actions are important These are the processes of absorption and scattering Thermal neutrons cause a stable isotope to become radioactive on exposure Since neutrons and hydrogen nuclei are of about the same mass the result of an elastic collision between two such particles will be the loss of roughly half of the neutron energy Radioactive isotopes may disintegrate by several methods, one of which is the ionization method of interaction of radiation with matter In this method a neutral atom splits into positive and negative parts Matter in the solid liquid or gas state can be ionized by charged particles provided they possess sufficient energy to eject electrons from the particular atom or molecule under consideration Biological damage due to radiation is a consequence of ionization in the body tissue

Three types of interaction between photons and matter occur (1) Photoelectric effect (2) Scattering (this has two varieties the Compton type and the coherent type) (3) Pair production In the photoelectric process all of the energy of the photon is transferred to an inner orbital electron of an atom In the scattering process there is (a) the Compton type in which the photon may collide with an electron and impart part of its energy to it and (b) the coherent type where the photon bounces off the atom or molecule changing direction without losing energy

The following points must be considered For alpha and low beta radiation the damage would produce a large dose in the deeper layers of tissue A roentgen equals 83 erg absorbed per gram of air In soft tissue the amount of energy absorbed per gram is approximately the same as air Units of measurement based on time are roentgens per minute and milliroentgens per hour

Rubber gloves protective clothing and nonabsorbent footwear should be worn In case there is danger from airborne contamination

of beta emitters into the body necessitates the use of sensitive detection equipment in evaluating the hazard due to contaminated surfaces and to contaminated air

The fundamental purposes of protective measures in handling radioisotopes are the following (1) To prevent ingestion, inhalation, and interstitial or other modes of entry into the body (2) To reduce the amounts of external irradiation to permissible levels There is a wide difference in the hazard created by absorption of various radio isotopes into the body Doses of radium and plutonium that are currently considered safe are radium, 0 1 microgram fixed in the body, and plutonium, 0 5 microgram fixed in the body Where sources are of low intensity the danger to the eye is not great Even for small amounts of activity it is often necessary to fabricate protective modalities to fit a specific situation In the effort to increase the distance between the eye and the source of radiation, care should be exercised in the design of shielding equipment Procedures employing new tools should be rehearsed with inactive material before work with active material is begun

The fundamental purpose of protective measures in dealing with sources of radiation which represent an external hazard only is to reduce amounts of external radiation to permissible levels If the eye is exposed to more than one type of radiation in a given weekly period, the total exposure from all components should not exceed 0 3 REM In the case of exposure of the eye and forehead to various types of radiation, the total dose from all components should not exceed 1/5 REM in a given period of one week

Under certain conditions, a vacuum tube can produce x rays of considerable intensity Any device in which electrons are accelerated is a potential source of x rays and should be checked in operation to determine if a radiation hazard exists

In general, devices employing high accelerating voltages and high electron currents are potent x ray sources The biological manifestations or symptoms due to either external or internal low level radiation exposure may be delayed for long periods of time This renders the immediate estimation of damage difficult Present practice consists of following the persons physical condition by conducting a complete physical examination before, during, and after work with sources of radiation

The decontamination of a surface that has been contaminated with radioactive material is a very difficult procedure In many cases it is advisable to remove that part of the surface that has become contaminated and treat it as radioactive waste This is especially true of porous surfaces because it is next to impossible to decontaminate them completely If the type of work being done requires quantitative counting of samples, the tolerable contamination may be smaller than the permissible level recommended for personnel protection

Correlation between the static and kinetic visual acuities of F 86 D pilots and police officers of the highway patrol was measured This data indicates that the static and kinetic visual acuities are not always proportional Both visual acuities of ordinary civilians differ more markedly than those of a man in specialized profession A comparison of this data with that in the preceding data emphasizes the superior kinetic visual acuity of the jet pilots

The kinetic visual acuity of a subject decreases in proportion to an increase in the velocity of the moving object that is being viewed In this result individual differences also may be recognized

After fatigue was introduced by subjecting the subject to a physical work load the kinetic visual acuity of the subject decreased noticeably *especially at the higher velocities of the visual object* This tendency also can be observed when the subject is suffering from lack of sleep mental exhaustion and so on

The variation in the kinetic visual acuity of a pilot before and after a flight in a jet plane was noticeable Although the decrease in the kinetic visual acuity after each flight is slight repeated measurements show a gradual decrease in the acuity therefore the decrease in the pilots kinetic visual acuity is not recognized by the pilots themselves because their static visual acuity remains the same

The correlation between the kinetic visual acuity of pilots and their self determined appraisals was proportional though only a few pilots had been interviewed The same correlation was seen in police officers of the highway patrol The officers having a poor kinetic visual acuity usually have poor records and have accidents more frequently

As was previously mentioned the kinetic visual acuity is an important function of the eye for pilots and we believe that our Kinetic Vision Tester will play an indispensable role in a quality test for a pilot in the detection of his physical condition and in the measurement of his fatigue

Several factors in the physiological mechanism concerning the difference between the static and kinetic visual acuities are presumed namely that the speed of accommodation and the minutely accommodative oscillation a term which have recently coined may take a part in the production of kinetic visual acuity

The amount of time necessary for a subject's eyes to accommodate on an object directly in front of him at distances of from five to thirteen meters was measured and indicated that the accommodation time was proportionate to the visual distance rather than to the accommodative amount

The experiments were performed in such ways that the moving object was exposed for a short yet constant time and during that time the perceptible limiting distance was measured in two methods The one shows the results when the exposure apparatus was attached to the visual object part and the other showed the data when the exposure

properly designed respirators should be employed Airborne contamination can be minimized by keeping the surface moist No person must be exposed to more than 0 01 microcuries per liter by air inhalation Particulate matter (Carbon 11) can also be filtered from the exhaust air Not more than two curies of radium, plutonium, or other members of the radium family, and not more than 11 disintegrations per second of all other radioactive materials may be packaged in one outside container for shipment by air except by special arrangement There must be no leakage Studies are now being carried out throughout the world to decontaminate persons exposed to sudden acute effects of radioisotopes The type and amount of medication used will be based on monitoring of areas in space flights The first of these medications will be in the form of excretory stimulants Later, drugs will be developed to change the chemistry of gamma emitting substances

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ABOUT THE IMPORTANCE OF KINETIC VISUAL ACUITY AGAINST ABILITY FOR PILOT

SUZUMURA AKIHIRO

Research Institute of Environmental Medicine
Nagoya University, Japan

It is a fundamental necessity that pilots must be able to see moving objects clearly and quickly Hitherto it was supposed that the difficulty experienced in seeing a moving object was due to the fact that the object moving, depending on various visual functions and in particular on the visual acuity of the object at rest

From the results of many experiments we have come to the conclusion that 'seeing' a moving object cannot be explained merely by seeing the static object, that is the object at rest, but that it depends upon another visual function which differ from the function involved when seeing the static object We have named this new visual function Kinetic Visual Acuity This term indicates the central or parafoveal visual acuity for a moving object that is approaching in a plane perpendicular to the transverse axis of the eyes We also have been able to produce a new apparatus for measuring Kinetic Visual Acuity which we have called a Kinetic Vision Tester

Now, we shall discuss several facts relating to how the perceptibility of a moving object is important to pilots

The subject, by using the optical system, can see the object that is approaching the eye in a plane perpendicular to the transverse axis of the eyes from one to twenty meters at various velocities

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exudations varying from narrow parallel sheathing to extensive extravasations, occur Generally one sector of the retina is believed to be involved As the disease progresses the haemorrhage in the vitreous gets absorbed but before the *vitreous has completely cleared up* another haemorrhage occurs The duration between two attacks increases, the haemorrhages become less frequent and they may cease altogether The phase of recurrent haemorrhages is either accompanied or followed by neovascularization and development of irregular and new anastomotic channels Ultimately retinal fibrous proliferation, retinitis proliferans and traction retinal detachment complete the sad story resulting in *permanent blindness In 11 cases the patients came* with history of blurring of vision On ophthalmoscopy the vitreous was normal and no apparent abnormality of the retina was seen, except that there seemed to be a small discontinuity in one or more of the retinal veins Sometimes one of the main branches, while at others a smaller branch of the retinal veins showed this discontinuity (Fig 6) These cases were not diagnosed as cases of Eales's disease Later these cases came with a typical attack of Eales's disease (Fig 7) This gave us a lesson that if in a susceptible case one encounters fullness and tortuosity of veins with evidence of discontinuity in their course, the cases should be diagnosed as one of Eales's disease and an adequate therapeutic regime should be enforced

In 29 cases where the patient complained of symptoms only in the affected eye, an ophthalmoscopic examination of the other eye revealed the presence of *retinal haemorrhages* in the periphery in one or more quadrants These cases eventually progressed to vitreous haemorrhages It seems, therefore, that the haemorrhages at first are confined to the retina but eventually a haemorrhage of sufficient magnitude occurs to burst through the internal limiting membrane to find its way in the vitreous This also suggests that a careful search for any evidence of periphlebitic reaction should be made in the *apparently normal eye in Eales's disease*

In our series we have seen that in 42 cases more than one vein was involved (Fig 8) and in several of these cases at least one small vein was involved in each quadrant (Fig 9) We are quite certain that if careful scanning of the fundus of Eales's disease is made most of the cases will show multiplicity of periphlebitic reaction The multiplicity of lesions may account for the failure of surgical measures adopted in this disease We feel that the disease is revealed in 4 stages

I A stage of venous dilatation tortuosity and discontinuity which may be due to an anoxic venospasm

II A stage of organic changes in the veins leading to periphlebitic vascular response and retinal haemorrhages

III A stage of recurrent vitreous haemorrhages and

IV Stage of retinal gliosis, retinitis proliferans, traction detachment and complete blindness

the examination of their flight possibilities at different high altitudes These tests consisted in subjecting them in the barochamber to depressions corresponding to the following altitudes 5 000 12 000 and 15 000 m, and then after the ground training test in a height compensating costume they are subjected in the same costume, to depressions corresponding to the altitudes of 14 000 16 000 and 18 000 metres Starting from 12 000 m oxygen was administered These seven tests were carried out each on a separate day, with a two days rest between the tests

During these tests our examinations were systematically centered on *the aspect of retinal vessels minimum blood pressure in the central retinal artery pulse general arterial blood pressure* comparatively before and after entering the barochamber, during the stay in the barochamber at various time intervals (always the same for the same altitude) and immediately after the egress from the barochamber a situation somewhat equivalent to landing We mention that the examination of the eye fundus even during the hypopressure in the barochamber was carried out through the 2 5 cm thick visor of the barochamber to which the aviator approached his eye as much as pos ible just as we did with the ophthalmoscope We may also mention that the retinal and general blood pressures have been recorded before the aviator entered the barochamber and immediately after his egress from it

The tests were carried out on 54 aviators between the age of 21 and 35 These tests totalized 2 406 examinations in all the above mentioned experimental variants

THE RESULT OF RESEARCHES

The researches have yielded the following data

1 *The aspect of the retinal vessels* A generalized and transient rapid retinal arteriolar spasm sets in at visibility limit with the increase in the calibre of retinal veins At the end of the 5 000 m test the venular dilatation remains unchanged for yet another short time after the egres from the barochamber which coincides with Mercier and Duguet s(3) observations which show that subjecting young men to fictitious altitudes of 6 000 m obtained in a barochamber, a retinal vasodilatation was ascertained

Generally in all the tests necessitating the administration of oxygen together with the discreet sustained spasm of retinal arterioles and the retinal venular dilatation a spontaneous pulse appears in case it does not already exist or it is being accentuated in case it normally and discreetly pre exists This situation becomes more evident in the case of ascents necessitating the administration of oxygen

2 *The minimum retinal blood pressure* On the ground (before entering the barochamber) it was generally comprised between the normal ground limits of 25–30 g (Baillart) while after the egress from the barochamber it had increased with the height of the ascent being generally comprised between 40–65 g (fig 1 2 3 4)

apparatus was attached ocular part however, *in the latter case no* measurement could be obtained. Thus, it may be said that accommodative speed to follow the movement of the object is necessary in order to have kinetic visual acuity.

The police officers after highway patrol duty experience a prolongation of their accommodation time and that the accommodation time of the officers having a low kinetic visual acuity is twice that of those having a good acuity. It also shows that as the kinetic visual acuity becomes lower the accommodation time increases.

From these results it may be presumed that in the production of kinetic visual acuity, whether it be high or low, the speed of accommodation and the minutely accommodative oscillation are factors which play an important role.

RETINAL ANGIO DYNAMIC ASPECTS IN CONDITIONS OF HYPOBARISM IN HIGH ALTITUDE PILOTS

M. CARAPANCEA, M. POPESCU, I. PINTILII, M. STOIAN and ST. MIHAI

(Roumania)

The visual apparatus is in a position to point out, at a detailed investigation, and by the disturbance of the delicate mechanism it consists of, not only the degree of local ocular disorders but especially—and this fact constitutes a preoccupation in the functional state of the entire organism—*the ocular response to general reactions*, under this latter aspect, by their graduated precision, ocular modifications adopt the aspect of a real biological titration of the complex behaviour of the organism.

The retinal arteriole, endowed with a much more voluminous wall, in comparison to its *blood* column, achieves the reverse of the situation of the humeral artery, in which the blood column predominates over its thin wall. Hence, it results that the humeral artery only *records the blood pressure* at a certain moment, while the retinal arteriole also and simultaneously records the parietal tonus which brings about visible ophthalmoscopic modifications, indicating past and present hypertensive stages, with their evolution.

In our researches we intended to examine whether and to what extent the retinal vessel can be modified *in conditions of hypobarism* in the barochamber, equivalent to the flight at various high altitudes.

RESEARCH TECHNIQUE

The researches were carried out at the Aviation Medical Center during the tests to which aviators are *normally subjected in* view of

The phenomena observed in aviators during hypopressure resemble to those pointed out by one of us in the rabbit subjected to hypobarism(2) In those researches it is shown that hypobarism induces a rapid retinal and carotidian arteriolar spasm followed by a stable retinal and carotidian arteriolar dilatation accompanied then by the respective venular dilatation No doubt that the phenomena observed were due to the experimental hypopressure permitted on the experience animal which succumbed immediately after

Of interest is the parallelism of experimental phenomena identical to a certain point with the clinical ones

As a matter of fact these experimental findings were confirmed by the still unpublished researches carried out by Acad Prof Gr Benetato and co workers which have established, by the Rein and Gibbs s method of recording the circulatory flow the increase in the cerebral circulatory flow What we have shown is equivalent to the increase in retinal circulatory flow both experimentally, in the animal and clinically in the aviators

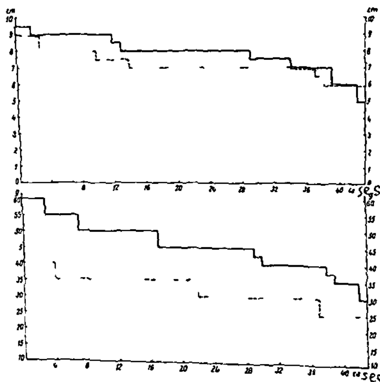


FIG 2

Above Minimum humeral arterial *tension* Below Minimum retinal tension On the ground (broken lines) and after the hypobari test at 12 000 m (continuous line)

3 *The pulse* It grew proportionally to the altitude, between 76–100–120/min

4 *General blood pressure* As against the ground one, after the ascent, it seldom maintained itself at the same level *In general it rose slightly*

INTERPRETATION OF RESULTS

We have shown that altitude hypopressure induces a fine, discreet, rapid, generalized and transitory arteriolar spasm at the limit of visibility, for the altitude of 5 000 m, and a constant one at altitudes which necessitate the administration of oxygen simultaneously with the arteriolar spasm appears a stable, consecutive, venulous dilatation, and usually a spontaneous venous pulse or its exaggeration in the case of its normal pre existence The return to the ground brings about, after a few minutes, the disappearance of the venous phenomena

The spontaneous venous pulse, however, becomes much more evident in ascents necessitating the administration of oxygen

These phenomena which occur at the level of retinal vessels, the smallest terminal ones, which can be directly investigated and which are anatomo physiologically equivalent to those of the central nervous system render the eye fundus examination as valuable as an indirect cerebroscopy

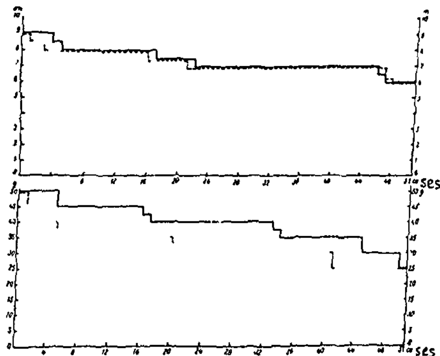


Fig 1

Above Minimum humeral arterial tension, Below Minimum retinal arterial tension On the ground (broken lines) and after the hypobaric test at 5 000 m (continuous line)

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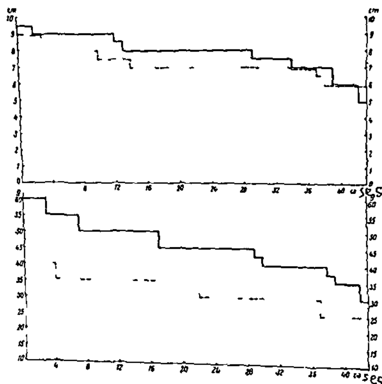


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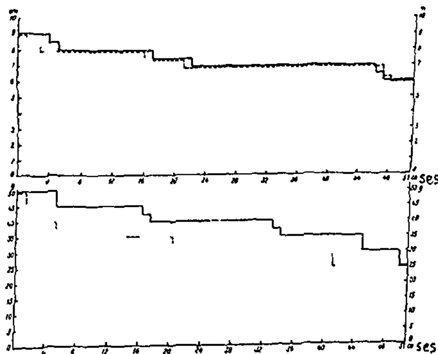


FIG 1

Above Minimum humeral arterial tension Below Minimum retinal arterial tension On the ground (broken lines) and after the hypobaric test at 5 000 m (continuous line)

Which is the explanation of the rapid arteriolar spasm which precedes the established vasodilatation—for the duration of the hypo pressure and subsequently extended for a short time—in the eye fundus?

The explanation should be looked for in the fact that the intraocular physiology is strictly dependent upon the nutritive requirements of the retinal cell Because of it the abnormally increased blood flow as against the nutritive requirements of the retina obligatorily deter mines from the very beginning a defence reaction manifested by the arteriolar contraction which impedes this surplus after which however the decompensation phenomenon of vasodilatation takes immediately place

What is the explanation of the venular dilatation in general and of the spontaneous pulse in particular, as well as its exaggeration in the ascent necessitating the administration of oxygen?

It is known at present that an excess of oxygen induces the spasm of the retinal arteriole

It seems easily understandable that a slight excess of oxygen induces the discreet spasm of retinal arteriole with a subsequent stasis in the retinal venules Concommitantly the ophthalmotonus, reduced at high altitude permits the passive increase in the calibre of the retinal venula and favours at the same time the increase in the venous pressure above that of the intraocular pressure which leads to the appearance of the spontaneous venous pulse The explanation of this phenomenon in the conditions of our researches must be looked for in the fact that the interocular pressure increases during the systole and flattens the venous wall situated under its own reduced pressure while in distole in which conditions are reversed the vein distends returning to its normal calibre

Thus in aviators the venous pressure is situated to the inter ocular pressure in conditions of a normally unstable equilibrium which imparts to the vascular wall rhythmic pressures from without inwards (intraocular pressure) and from within outwards (venous pressure) The exaggeration of the spontaneous venous pulse in the case of its normal pre existence is due to the fact that the relation between intraocular and venous retinal pressures are of a nature allowing the equalization of the flattening and expanding movements of the venous retinal wall

The disappearance of the spontaneous venous pulse shortly after the return to normal ground altitude is due to the fact that on the one hand oxygen ceases its action and on the other that ophthalmo tonus returns to its normal conditions previous to the ascent when it was constantly either higher or lower as compared to the retinal venous pressure a situation in which the venous pulse does not appear

The minimum retinal pressure was raised which shows that though the aspect of the retinal artery is normalized as seen on the ophthalmoscope there still existed a short time after the return to

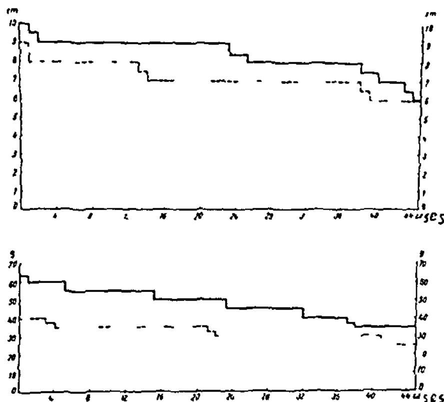


Fig 3

Above Minimum humeral arterial tension Below Minimum retinal arterial tension On the ground (broken lines) and after the hypobaric test at 15 000 m (continuous line)

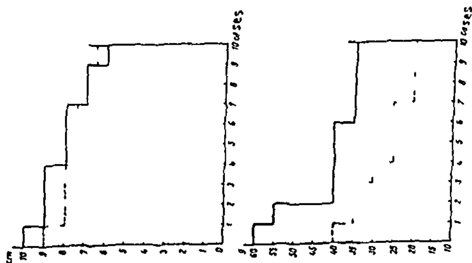


Fig 4

Above Minimum humeral arterial tension Below Minimum retinal arterial tension On the ground (broken lines) and after the hypobaric test at 18 000 m (continuous line)

In this connection we must underline the fact that our present point of view in considering the angio retinal modifications, included completely among the disturbances of the cardio vascular apparatus is no doubt, generally speaking justified

However, the existence of an eventual individuality of the cephalic vascular sector might modify fundamentally our point of view in connection with the functional phenomena of this region during general arterial hypertension

This hypothesis has been suggested by the results of the complex researches carried out by Acad Prof Gr Benetato and co workers in 1956(1) on the variations of the circulatory flow and the cerebral oxygen consumption in the dog in relation to the general circulatory flow and the total consumption of oxygen under the action of various drugs The findings of these researches regarding the action of *atropine* and of hystamine argue against the conception which predominated for a long time in physiology and clinical pathology, according to which the cerebral circulation is passively regulated only by the variations which occur in the general circulation at the same time they plead for the ununiform repartition along the vascular tree of the tonic sympathetical parasympathetical action with the predominance of the parasympathetic tonus at the level of the cerebral vessels

The Laboratory for Clinical and Experimental Physiology and Physiopathology of the Eye of the Normal and Pathological Physiology Institute Daniel Danielopolu of the Academy of the Rumanian People s Republic

Director of the Institute Acad Prof Dr Gr Benetato

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MODIFICATIONS OF THE VISUAL ACCOMMODATION IN CONDITIONS OF HYPOBARISM IN HIGH ALTITUDE PILOTS

by

M CARAPANCEA M POPESCU, I PINTILIE M STOIAN, V TEODORESCU and M STEFAN

(Roumania)

Present flight conditions induce in aviators two states of myopia anoxemic and altitude or spatial myopiae *Anoxemic myopia* — occurring

conditions of normal, ground, pressure, a slight *increase in pressure*, *which sometimes coincides with the increased general pressure*. We used the expression *sometimes*, and underline this fact, which *signifies that the cephalic segment blood pressure in aviators, was still on the ground, in conditions of hypertension and subsequent local stasis, as against the rest of the organism subjected to a normalized blood pressure*.

PRACTICAL CONCLUSIONS

Vascular modifications of the eye fundus, induced by altitude hypopressure still persists a short time after the return to normal, ground pressure.

The only *immediate action which venous intraocular stasis can have, in the meantime, upon any of the functions of ocular viscera is that upon the activity of the ciliary muscle*.

In fact, so long as the interocular venous stasis lasts, so does undoubtedly also the one in the musculo vascular region of the ciliary zone, and more precisely of the portion of ciliary process.

It results that the venous *stasis in the ciliary muscle can but only hinder the normal functioning of the latter, i.e., hinder to a certain extent the amplitude of its normal contraction*.

This situation is particularly accentuated in the case of the hypermetropic accommodation, which has a *permanent* character. In fact the accommodation of the hypermetrope is the capacity of *continuous modification* of the refraction of the crystalline lens *to any distance* — since *punctum remotum* is virtual and placed beyond the infinite, while *punctum proximum* is placed behind the retina — subsequent to states of graduated contraction — relaxation of the ciliary muscle, transmitted by the intermediary of Zinn's zonule to the crystalline capsule, so that the eye's image be formed *always, mathematically on the retina*, starting from infinity to a distance of a few centimeters from the eye.

Thus, the aviator cannot accommodate in normal conditions during *the landing operation of the very rapid modern aeroplane*, when the pilot is obliged to adjust both the *image of the ground* which approaches very rapidly, and the *image of the board apparatus* placed at a constantly fixed distance.

In any case, in view of the above considerations, the systematic investigation of the pressure in the central retinal artery becomes compulsory, both in engaging navigating pilots and in periodical medical controls of barochamber tests, they are submitted to.

Thus, since present researches have underlined the fact that on *the ground the minimum retinal blood pressure has maintained itself raised in a normal ophthalmological field and in a normal general tensorial state, hence* the deduction that on the ground, the blood pressure of the *cephalic segment* was still in a state of hypertension as against the rest of the organism submitted to a normalized vascular pressure.

XIX CONCILIUM OPHTHALMOLOGICUM

ACTA

(Under patronage of the Government of India)



Fig 6 (A S)
A S Showing Discontinuity of Superior Temporal Vein



Fig 7 (A S)
A S Later in an attack of Haemorrhage along Superior Temporal Vessels and in the vitreous

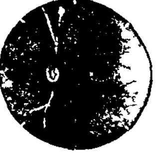


Fig 8 (P C T)
P C T Showing involvement of two big veins



Fig 9 (V S)
V S Showing involvement of one vein in each sector

In our researches we intended to find out whether and to what extent may visual acuity be modified in conditions of barochamber hypobarism equivalent to the flight at high altitudes

It is important that this phenomenon be studied since in present flight conditions it represents for the aviator the essential element in piloting the plane

RESEARCH TECHNIQUE

Researches were carried out at the Medical Aviation Centre during the tests to which aviators are normally subjected in view of examining their flight possibilities at different high altitudes These tests consisted in submitting them in the barochamber to depressions corresponding to the altitudes of 9 000, 12 000 and 15 000 metres and then after ground training tests in a height compensating costume they are subjected in the same costume to depressions corresponding to the altitudes of 14 000, 16 000 and 18 000 metres These seven tests have been carried out separately with an interval of two days between them

During these tests we have followed systematically the achromatic and chromatic static and dynamic visual accommodation of the comparative *punctum remotum* before entering the barochamber during the stay in it at various intervals (always the same for the same altitude) and immediately after the egress from the barochamber a situation somewhat equivalent to landing

The visual accommodation in the variants shown above has been investigated by the intermediary of some black and coloured letters of various dimensions corresponding to various hypernormal and normal visual acuities fixed on a paper band rotating on a kimograph at a speed of 500 mm /sec This kimograph was placed at the prescribed distance for determining visual acuity the examination of the perception of letters was also followed in barochamber hypopressure atmospheric conditions the pilot reading on the microphone the same letters which he saw this time — at the same distance — through the barochamber visor The movement of the letters on the kimograph band has simulated a situation similar to that of the sudden appearance and disappearance of images which might appear during high altitude flights in conditions of a somewhat similar estimation of speed and distances

We then followed systematically before and after the egress from the barochamber the dynamic visual accommodation of the clearest *punctum proximum* by measuring the distance between the retina and the nearest and most distinct visual point For this purpose the aviator sitting on a chair with the back to the window, looked successively with each eye at the letter on an octotype for the near sight the letter being gradually brought nearer up to the limit at which its clear perception began to become slightly cloudy For the commodity of the researches the proximometer conceived by M Carapancea and M

under the influence of the diminution of the oxygen in the blood, "markedly reduces — *according to Mercier and Duguet(2)* — accommodation amplitude." Along the same line, it was shown that *after an hour's exposure in a plane*, on a mountain, or in the baro chamber, to a 5 000 m altitude, 10 minutes are necessary for the accommodation to return to normal(1). *Altitude or spatial myopia* has been noticed in numerous U.S.A. pilots and observers, after 5–8 years of flight, hence the conclusion that emetropia does not ensure a permanent visual efficiency, but that only weak hypermetropia *is a protection* against this acquired myopia. The explanation of this professional ametropy *has been identified, according to Mercier and Robert(3)*, and Mercier(4), in the special state of accommodation induced by *staring at a* visual field completely devoid of details. In fact, it is well known that in the presence of an "empty" visual field, lacking all guide marks, achieved by perfect darkness, *uniform fog, cloudless sky* considered by clear atmosphere, as is the perfectly mat white screen of the high altitude sky, the eye is adapted for a *punctum remotum* corresponding to the "imagined" distance of 1–2 metres, with a special myopia of about 1 d.

In the case of the pilot, who should preferably be not an emetrope, but a hypermetrope, i.e. having a supernormal sight for great distances, the ciliary muscle is super stressed by the accommodation activity, an effort continuously imposed for the far sight (even the sight to infinite — since *punctum remotum* is virtual and situated beyond the infinite) — as well as, and particularly for *the near sight* as *punctum proximum* — is placed at the back of the retina. Thus, the hypermetrope's *sight is never distinct, whatever the distance to the object considered*, except by a continuous accommodative effort, which ensures the stability of a clear sight. *Thus, in the hypermetrope, the adaptation* of the image, both for far sight, as well as for near sight, has the aspect of a continuously active phenomenon.

The *number of accommodative acts, however*, which are required of a pilot, is outright impressive. Platonov(5) writes: "Even on a *training plane, with a speed of about 100 km an hour, for a single lap* on the flight strip, from take off to landing, i.e. approximately 4 min., *the pilot is obliged to direct his attention 300 times from one object* to another, in a strictly determined succession. In the much more complex jet plane, with the increased number of necessary reactions and the reduced available time the working rhythm becomes more rapid." Platonov(5) also shows that, if the pilot *has a 1,5* visual acuity, he can identify an enemy plane which flies to meet him at the rate of 1 000 km per hour, from a distance of about 850 m.; if he has however, a visual acuity of 0,5, he will only be able to make it at a smaller distance (about 115 metres). If we consider the speed of each plane as equal to only 270 km/hr (The approaching speed will be of 540 km/hr), then the pilot with a 1,5 visual acuity will have at his disposal, *up to meeting moment*, 5,5 sec., while the pilot with a 0,5 visual acuity will only dispose of 3.7 sec."

from the barochamber a much closer *punctum proximum* than the one observed before the hypopressure thus an increase in the amplitude of accommodative contraction This nearing of the *punctum proximum* was usually directly proportional to the degree of the hypopressure at altitudes above 5 000 m If on the ground the accommodative amplitude was comprised between 6 and 16 cm after the return from the flight it was between 5 and 14 cm at 5 000 m between 5 and 13 at 12 000 m, between 5 and 12 at 15 000 m, between 5 and 10 at 16 000 m and between 4 and 8 cm at 18 000 m (Fig 2 3, 4, 5, 6)

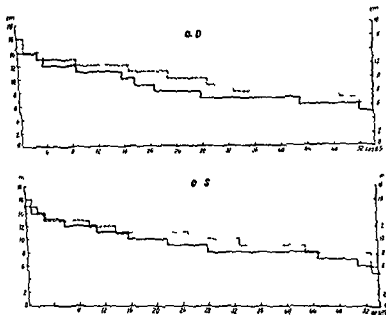


Fig 2
Punctum proximum on the ground (broken lines) and after hypobaric tests at 5 000 m (continuous lines) O D = right eye O S = left eye

We have also noticed that the *punctum proximum* is approaching much more in flight trained aviators and less *in lesser trained* ones much more in aviators trained at high altitudes than those trained at lesser altitudes

The duration of the maintenance of the close *punctum proximum* has varied between 5 and 15 *min* and was directly proportional to the degree of hypopressure in altitudes above 5 000 m to flight training and especially to training at high altitudes

3 Normal *pupillometry* The pupillar diameter was rarely reduced by 0 5 mm as compared to the one previous to the barochamber altitude test

Popescu permitted by a method easily understood by the investigated person, the simple, rapid and precise determining of the *punctum proximum* (Fig. 1)

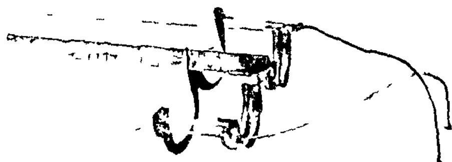


Fig. 1
M. Carapancea and M. Popescu's PROXIMOMETER

At the same time, the behaviour of the irian muscle was also studied by iridokinesimetry or pupillometry, consisting in the comparative measurement of pupillar diameters before and after the barochamber tests

Researches were carried out on 54 aviators between 21 and 35 years of age, totalizing, within the accommodation investigations a number of 2480 examinations in all the experimental variants described above while among investigations relating to pupillar modifications 382 examinations were carried out

THE RESULT OF RESEARCHES

The researches carried out have yielded the following results

1 *Achromatic and chromatic, static and dynamic visual accommodation of the punctum remotum* Before and after the altitude test, in the barochamber, *this accommodation is normal* while within the barochamber, at a hypopressure corresponding to altitudes of 5 000 and 12 000 m, in 21 out of the 54 aviators, the confusion of the colour of blue letters, perceived at 5/7 and 5/3 acuities, with that of black letters of the same dimension has been observed

2 *Dynamic, visual accommodation of a punctum proximum* Our proximometer has almost always emphasized immediately after the egress

hypopressure The clearest *punctum proximum* determined with the proximometer is the more nearing the eyes the more the hypo pressure corresponds to altitudes above 5 000 m and at the same time the more the aviator is trained in flight and especially in high altitude flights

These facts suggest the following explanations

1 In conditions of barochamber hypopressure which induces the nearing of the *punctum proximum a constant increase in the amplitude of crystalline refraction sets in subsequent to a proportional increase in the accommodative contraction of the ciliary muscle which is in a state of spasm* Under

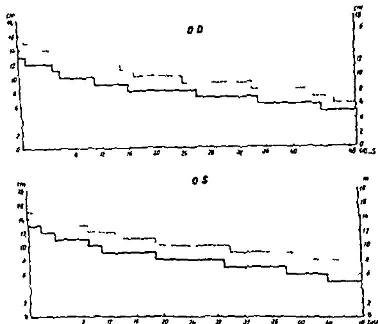


Fig 4
Punctum proximum on the ground (broken lines) and after hypobaric tests at 15 000 m (continuous lines) O D = right eye O S = left eye

the influence of hypopressure and in proportion to it the ciliary muscle is fixed in a state of exaggerated accommodative contraction as against the one recorded previously on the ground where pressure was normal The state of hypobarism accommodative contraction justifies the corresponding situation of the crystalline lens with a refringency of a myotic type which necessitates the perception of the *punctum proximum* at a smaller distance than that of the crystalline lens with normal refringency ordered by an uncontracted ciliary muscle in conditions of normal ground atmospheric pressure

INTERPRETATION OF RESULTS

The non coloured and coloured visual accommodation of the fixed and mobile *punctum remotum*, necessitating the adjusting of its image from the static and dynamic *point of view*, was *normal* before, during and after the barochamber altitude tests

We have, nevertheless, established *in* 21 *out of the* 54 *aviators* that in barochamber hypopressure, corresponding to the altitude of 5 000 m , the confusion of blue with black, for both subnormal (5/7) and hypernormal (5/3) visual acuities, has *taken place*

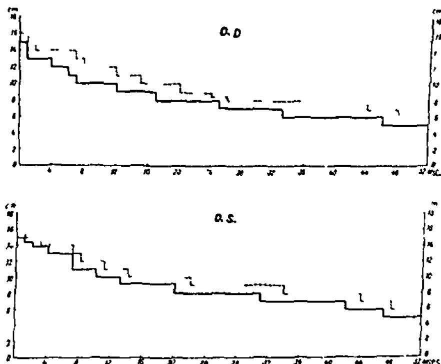


Fig 3

Punctum proximum on the ground (broken lines) and after hypobaric tests at 12 000 m (continuous lines) O D = right eye O S – left eye

Our observation tallies with Platonov's (5) which shows that colour sensibility decreases slightly even at the slightest oxygen insufficiency, when *the pilot* begins to differentiate with *difficulty* certain colours and shades It should be kept in mind that the decrease in colour sensibility begins sometimes even at the height of 2 000 to 5 000 m" Platonov (5) concludes That is why in particularly important reconnaissance flights, oxygen should be used not as from 15,000 m but from a much *lower* altitude '

Visual accommodation of a mobile *punctum proximum*, necessitating the adjustment *of its* dynamic image, evolving between the near and the nearest clear vision is plainly modified by high altitude

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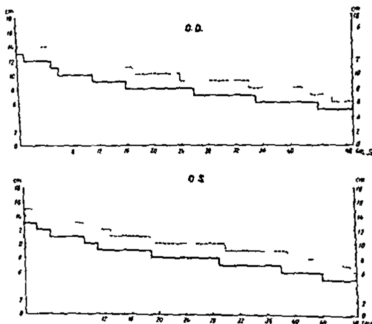
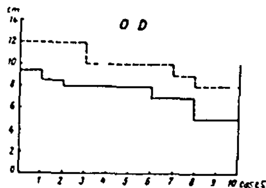


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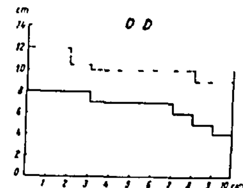


Fig 5

Punctum proximum on the ground (broken lines) and after hypobaric tests at 16 000 m (continuous lines) O D right eye O S left eye

Fig 6

Punctum proximum on the ground (broken lines) and after hypobaric tests at 18 000 m (continuous lines) O D – right eye O S = left eye

For this transient emetropia induced by hypobarism, we propose the name of *hypobaric myopia*

At the beginning of the present paper we have stressed the present importance of the state of *anoxemic myopia* and *spatial or altitude myopia*, in the ocular physiology of the aviator

We have, however, established, that in aviators, — in the impossibility of achieving spatial myopia — beginning by keeping him at a barochamber altitude of 5 000 m, without the inhalation of oxygen and then raising him to higher altitudes, when the inhalation of oxygen *is compulsory, the accommodation contraction was proportionally accentuated* with the altitude attained

The following conclusion becomes evident if at 5 000 m hypoxemia acts together with hypobarism, at altitudes above 5 000 m, where hypoxemic action decreases, and that of hypobarism increases, this decreases predominantly the accommodation amplitude

Thus — by the examination of the aviator, more subjected to hypopressure, decreasing the degree of anoxemia and eliminating the existence of any imaginary *punctum remotum*, both possible generators of myopia — our researches disclose a new altitude emetropia *the*

altitude hypopressure myopia which *sets in immediately and disappears shortly* after the ceasing of the hypopressure action

2 Hypobaric myopia lasted between 5 and 15 minutes Its duration was directly proportional to the degree of hypopressure of altitudes above 5 000 m, with flight training especially at high altitudes

The fact that the duration of hypopressure myopia is directly proportional to the degree of hypopressure above 5 000 m only underlines the greater intensity of the stability of ciliary spasm phenomenon under the influence of hypopressure

The fact that the duration of hypopressure myopia is directly proportional both to the flight training and to high altitude training, only underlines the adaptation promptitude of the ciliary muscle, probably hypertrophied in the meantime after the numerous solicitations of repeated hypopressures

In these conditions it seems beyond doubt that *altitude hypobaric myopia* is an important helping factor to the two myiopiae

There is apparently a contradiction in our experiences which show on the one hand that accommodation of the *punctum remotum* is realized normally while that of *punctum proximum* emphasizes a state of myopia

The contradiction is merely apparent

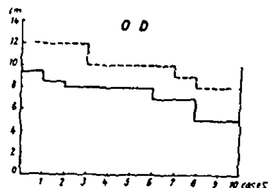
The distant sight is normal but the sight between *punctum remotum* and *punctum proximum* is that which is influenced by *myopia set in by* the influence of hypopressure This altitude hypobaric myopia is all the more pronounced as the sight approaches *punctum proximum*

In this connection it is interesting to point out the fact of observation that the depth or stereoscopic acuity — connected with illumination precision of outlines *and the distance* of objects perceived binocularly as two slightly different retinal images — is according to Platonov (5) influenced in *aviators by the* insufficient oxygenation of the blood Therefore after a high altitude flight it is recommended that before landing one or two tours of the landing strip be made (Platonov)

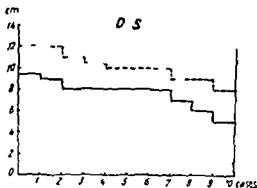
PRACTICAL CONCLUSIONS

Disturbances of chromatic confusion of blue and black are only due to altitude hypoxia hence — as shown by Platonov (5) — the imperative necessity that in particularly important reconnaissance flights oxygen be used not from 4 500 m but from a much lower altitude

Altitude hypopressure myopia which we point out to for the first time, — sets in immediately and disappears shortly after the action of hypopressure It undoubtedly contributes considerably to the setting in of the state of altitude myopia by *imagining a very near punctum remotum* which in time becomes stable and irreversible







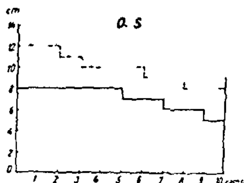


Fig 5

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examination technique was based on the punctiformous pressing of the hair, its curving thus achieving an elastic force which exercised a counter pressure which could be measured by the similar pressure on the dish of a balance Von Frey s method required however hairs of different lengths calibres and elasticities, depending on their age a fact which constituted an important impediment for its clinical application On the other hand the constancy of the hair s force varied in its turn with atmospheric humidity These two serious inconveniences have impeded the spreading of von Frey s method

Ingenious forms of apparatuses for determining these sensibilities have been conceived but in the course of time, they all have been proved inexact

The current method of bulbar conjunctival and corneal sensibility investigation has, therefore still remained the one which uses the touching of the eye with a finely twisted cotton wool pad in the form of a pointed brush The touch (single stimulus) or the stroking (multiple and unequal stimuli) with cotton wool induces a more or less painful sensation in equal or more accentuated intensities in one part or another of the respective explored region as subjective phenomena and a blinking reflex as an objective phenomenon

In 1952 in his thesis About the Corneal Sensibility , Jorn Boberg Ans (2) (3) has suggested a variant improving von Frey s method which consisted in replacing the hair by a nylon thread which has constant physical properties is round and uniform Thus the elasticity coefficient of the nylon thread with a 0,112 mm diameter and a length between 5 and 55 mm, achieves the series of pressures required for the measurement of corneal sensibility Introduced into a special telescopic system this thread permits the variation in the length of the nylon thread The author has computed the force (P_E) which acts at the end of the elastic nylon thread by Euler s formula

$$P_E = \frac{\pi^2 E I}{l^2}$$

In this formula l being the length of the thread

I (inertia) $= \frac{\pi^2 \ d^4}{64} = 0\ 049\ d^4$ in which d (diameter of the thread) being 0,112 mm, the result is $I = 0\ 72\ 10^{-9}\ cm^4$ E (elasticity coefficient) in a nylon thread with L (length) and d (diameter) may be computed in variable conditions thus

with 0% relative humidity	E being $4\ 92\ 10^4$	P_E	$= \frac{710}{L^2}$ mg
50%	,, $3{,}16\ 10^4$	P_E	$= \frac{450}{L^2}$ mg
100%	,, $1\ 19\ 10^4$	P_E	$= \frac{170}{L^2}$ mg

Hypobarism myopia is directly proportional to the degree of hypobarism, flight and high altitude training, which imply in the first case the intensity of the ciliary spasm, and in the other two,— according to the aviator's training — the prompt adaptation of the ciliary muscle, probably hypertrophied after the numerous solicitations of reiterated hypopressures

It results in that the pilot who has become myope in conditions of high altitude flights cannot accommodate himself in normal conditions during the landing of present very rapid planes, when both the image of the ground which approaches very rapidly, and the image of the board apparatus, situated at fixed, constant distance, have to be adjusted

The Laboratory for Clinical and Experimental Physiology and Physiopathology of the Eye of the Normal and Pathological Physiology *Institute* "Daniel Danielopolu" of the Academy of the Rumanian *People's Republic* Director of the Institute Academician Prof Dr Gr Benetato

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by

M CARAPANCEA, M POPESCU L RAIIU, I PINTILIE M STOIAN and M SILIAN

(Roumania)

PREVIOUS RESEARCHES

The examination of the sensitivity of bulbar conjunctiva and cornea was previously carried out by touching them with a finely pointed bit of cotton wool

In 1894, this inexact method had already been replaced by von Frey's, which employed hairs of various calibres and lengths His

examination technique was based on the punctiformous pressing of the hair, its curving thus achieving an elastic force which exercised a counter pressure which could be measured by the similar pressure on the dish of a balance Von Frey's method required however hairs of different lengths, calibres and elasticities depending on their age a fact which constituted an important impediment for its clinical application On the other hand, the constancy of the hair's force varied in its turn with atmospheric humidity These two serious inconveniences have impeded the spreading of von Frey's method

Ingenious forms of apparatuses for determining these sensibilities have been conceived but, in the course of time they all have been proved inexact

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In our country, Dr Eugen Ratiu and Eng Anton Ivanovici have perfected the Boberg-Ans esthesiometer, by a guiding system of the thread inside the tube which contains it, thus averting the supplementary sliding of the nylon thread, as it happens in the Boberg Ans apparatus

In order to facilitate the reading of results, the authors have devised a table in which, in relation to the length in mm of the nylon thread, its mg pressure is shown, exercised according to the atmospheric humidity of the day in which the sensibility is examined, and since in Rumania humidity varies between 50 and 80%, calculations were marked for every 10% humidity, and between 50 and 100%

OBJECT OF RESEARCHES

It is a known fact that young people present an average bulbar conjunctival sensibility of 72–200 mg, and an average corneal sensibility of 15 mg or less in the center, and of 15–20 mg in the sclero corneal limbus *Corneal and conjunctival sensibilities decrease with age*

On the other hand, it is also known that intraocular pressure below 30 mm Hg (within limits considered as normal) does not determine any sensibility modification, while above 30 mm Hg, the corneal sensibility threshold increases equivalently by 18–20 mg, up to 50–72 mg, whence it evidently results that corneal sensibility varies with intra ocular pressure

Our researches had in view to establish whether and to what extent, bulbar conjunctival and corneal sensibilities appear modified in conditions of the return from hypobarism, having in view the fact that, on the one hand, that this induces important disturbances in the arterial pressure of the cephalic segment, as was shown, both experimentally (1) and clinically (4), and therefore implicitly in the conjunctival sector, while, on the other hand that ophthalmotonus decreases at high altitudes

RESEARCH TECHNIQUE

Our researches were carried out at the Aviation Medical Center during some of the tests which aviators are normally subjected to in view of the examination of their flight possibilities at different high altitudes These tests consisted in the aviators being subjected in the barochamber, to depressions corresponding to the altitudes of 5 000 12 000, and 15 000 metres, the last two tests being carried out with administration of oxygen Each of these three tests have been made on separate days, *with two days rest between the tests*

In our examinations we have employed the esthesiometer conceived by the two Rumanian innovators

Our investigations have only had in view the testing of the limitary sensibility threshold resulting from the slightest touch, and in verifying the reality of the perception of minimal sensation we made touch simulations

We have avoided possible technical errors by holding the handle of the apparatus exactly over the point of contact applying the thread at right angles to the bulbar conjunctiva and the cornea, taking care that the thread curbure does not exceed 5% of its free length The application of the point of the thread on the eye was made as slowly as possible so as always to have the same lightest and most constant excitation intensity, since the rapid application increases the effect of the stimulant

We recorded *for each eye separately* the minimum perception of the bulbar conjunctiva and then of the cornea, by the examination always in the same succession, of the sensibility in the four cardinal points of the paralimbic bulbar conjunctiva at 3 mm from the sclero corneal limbus (upper and nether by opening the palpebral slit with the thumb and the forefinger) and then by examining the sensibility always in the same succession in the four cardinal points of the paralimbic cornea and in the center of the cornea

The bulbar conjunctival and corneal sensibility has been recorded in aviators in conditions of normal ground pressure before entering the barochamber and immediately after the egress from it, where they had been subjected to the above altitudes

Our researches have been carried out on a lot of aviators of 21–35 years of age of whom not all had been subjected to all the tests The esthesiometry of the bulbar conjunctiva and of the cornea have thus been examined in normal ground conditions in 45 cases while immediately after the return from the altitudes of 5 000 12 000 and 15 000 metres respectively in 45 43 and 39 cases

The bi ocular researches — effectuated in normal ground conditions and immediately after the return *from the mentioned altitudes* investigating the bulbar conjunctiva in four regions and the cornea in five regions — have totalized a number of 3 096 results the respective computation of which has been related to the Bucharest humidity *during the period* May 30 and June 23 1960 when this esthesiometry has been practised

THE RESULT OF ESTHESIOMETRIC INVESTIGATIONS

Topographic esthesiograms of bulbar conjunctiva and cornea computed in mg pressure (Fig 1) show the following results

1 The esthesiogram of normal, ground bulbar conjunctiva is contained in O D (right eye) between 8 and 100 mg, *the mean* varying between 19 8 and 37 7 mg while the O S (left eye) between 12 and 100 mg *the mean varying* between 20 1 and 34 5 mg the threshold of this sensibility thus presenting a lower nether limit in O D than in O S (O D 8 mg O S 12 mg) while the upper threshold limit is the same in A O (both eyes) (100 mg) in comparing topographical sensibilities it is also noticed that in A O the nasal region is the seat of the highest sensibility threshold of the entire

In our country, Dr Eugen Ratiu and Eng Anton Ivanovici have perfected the Boberg Ans esthesiometer, by a guiding system of the thread inside the tube which contains it, thus averting the supplementary sliding of the nylon thread, as it happens in the Boberg Ans apparatus

In order to facilitate the reading of results, the authors have devised a table in which, in relation to the length in mm of the nylon thread, its mg pressure is shown, exercised according to the atmospheric humidity of the day in which the sensibility is examined, and since in Rumania humidity varies between 50 and 80%, calculations were marked for every 10% humidity, and between 50 and 100%

OBJECT OF RESEARCHES

It is a known fact that young people present an average bulbar conjunctival sensibility of 72–200 mg, and an average corneal sensibility of 15 mg or less in the center, and of 15–20 mg in the sclero corneal limbus Corneal and conjunctival sensibilities decrease with age

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Our investigations have only had in view the testing of the limitary sensibility threshold resulting from the slightest touch, and in verifying the reality of the perception of minimal sensation we made touch simulations

50 mg), comparing topographical sensibilities, it is also *noticed that* the higher and the lower region from O S have a *threshold comprised* between the same *sensibility limits* (12–84 mg)

4 Bulbar conjunctival *esthesiogram recorded immediately after the return from* the 15 000 m altitude, is comprised in O D between 18 and 450 mg the mean varying between 48 2 and 122 6 mg, while in O S between 16 and 450 mg, the mean varying between 44 7 and 117 8 mg thus, this sensibility *threshold presents a similar* upper limit in A O (450 mg) while the nether threshold limit is higher *in* O D than in O S (O D 18 mg O S 16 mg), comparing the topographic sensibilities it is also noticed that the temporal region of A O is the seat of the highest sensibility threshold of the entire bulbar conjunctival surface (450 mg) equally the temporal and nasal regions have similar sensibility thresholds (*temporal* A O 26 450 *mg* nasal A O 33–320 mg) while the higher and lower regions from O D, have a threshold contained within the same sensibility limits (18 112 mg) The corneal esthesiogram also recorded immediately after the return from the 15 000 m altitude is contained in A O between 15 and 84 mg the mean varying in O D between 29 2 and 33 mg while in O S between 29 3 and 35 7 mg, thus, this sensibility threshold presents in A O a both higher and lower limit identity comparing topographical sensibilities, it is noticed that the regions temporal from O D and the nether from O S are the seat of *a threshold contained within the same sensibility limits* (15–50 mg) and that the A O nasal regions have likewise a sensibility threshold contained within the same limits (16–84 mg)

The general mean of A O topographic esthesiograms (Fig 1) shows both in bulbar conjunctiva and in cornea a directly propor*tional rise in the mean sensibility threshold of all investigated regions*

The systematic rise in the extreme nether and upper limits of the sensibility threshold takes place up to 15 000 m where as compared to thresholds recorded at 12 000 m, we find that if the lower conjunctival region presents a lowered nether limit and a stationary *upper limit the higher lower* and temporal corneal regions present a lowered upper limit

The resulting general mean of the bulbar conjunctival and corneal global sensibilities computed in mg pressures (Fig 2) shows a rise in both sensibility thresholds, in proportion to the altitude from *which it returned but more* rapid and marked in bulbar conjunctiva than in cornea

Mean global sensibilities of *bulbar conjunctiva and cornea* reckoned in mg pressure, in 39 cases distributed in three category groups *identical* in both eyes starting from the bulbar conjunctival *sensibility recorded* as from 15 000 m to the ground (Fig 3*a*, *b*) point out to the following facts

The thresholds of both ocular *sensibilities exhibit — within their* rises proportional to the altitude from which they return, but more

bulbar conjunctival surface (100 mg) Normal, ground corneal esthesiogram is contained in O D between 8 and 28 mg, the mean varying between 12,5 and 13,1 mg, while in O S between 8 and 23 mg, with a mean varying between 12,5 and 13,2 mg, so that this sensibility threshold presents a higher upper *limit in O D*, *than in O S* (O D 28 mg, O S 23 mg), while the nether threshold limit is the same in A O (*8 mg*), *comparing* topographic sensibilities, it is also noticed, on the one hand, that the central region threshold is identical in A O, and, on the *other hand*, that in each eye the temporal and nasal regions, and the higher and lower ones have a threshold contained *between the same sensibility* limits (temporal and nasal O D 8–28 mg, higher and lower O D 8–23 mg, temporal and nasal O S 8–23 mg, higher and lower O S 8–19 mg)

2 Bulbar conjunctival esthesiogram, recorded immediately after *the return* from the altitude of 5 000 m, is contained in A O between 12 and 182 mg, the mean varying in O D between 29,7 and 7,31 mg, while in O S between 32,1 and 68,9 mg, so that this sensibility threshold presents in A O a limit identity, both higher and lower, comparing the topographic sensibilities, it is also noticed that in A O the nasal region is the seat of the highest sensibility threshold of the entire bulbar conjunctival surface (182 mg) The corneal esthesiogram also recorded immediately after the return from the 5 000 m altitude, is contained in O D between 8 and 50 mg, with the mean varying between 21,4 and 22,9 mg, while in O S between 9 and 50 mg, with the mean varying between 21,9 and 22,4 mg, thus the sensibility threshold presents a nether limit, slightly higher in O S than in O D (O S 9 mg, O D 8 mg), while the upper threshold limit is the same in A O (50 mg), comparing topographic sensibilities it is also noticed that in O S the temporal and nasal regions have a threshold contained between the same sensibility limits (9–42 mg)

3 Bulbar conjunctival esthesiogram recorded immediately on return from the 12 000 m altitude, is contained in O D between 18 and 182 mg, the mean varying between 41,9 and 87,3 mg, while in O S between 15 and 320 mg, the mean varying between 38,4 and 87,1 mg, this sensibility threshold thus presenting a higher upper limit in O S than in O D (O S 320 mg, O D 182 mg), and a higher nether limit in O D than in O S (O D 18 mg, O S 15 mg) comparing topographic sensibilities, it is also noticed that in the A O nasal region is the seat of the highest sensibility threshold of the entire bulbar conjunctival surface (O S 320 mg O D 182 mg), while the O D higher and lower regions have a threshold contained between the same sensibility regions (18–100 mg) The corneal esthesiogram also recorded immediately after the return from the 12 000 m altitude is comprised between 12 and 50 mg, the mean varying between 25,5 and 27,6 mg, while in the O S between 12 and 84 mg the mean varying between 27,9 and 31,4 mg, this sensibility threshold thus presenting a similar nether limit in A O (12 mg), while the upper threshold limit is higher in O S than in O D (O S 84 mg, O D

THERAPY

The treatment of Eales s disease has been unsatisfactory Various therapeutic measures like iodides, thyroid, oestrogens, vitamin C, vitamin K and vitamin P have been used in the past but without any benefit Results with antitubercular drugs have been disappointing Belz and Bouche (1951)[25] recommended ultrasonics to disperse the blood clots but the fate of this therapy has in no way been better than those preceding it Guyten and Reese (1948)[26] and many others have claimed good results by X ray and radiation therapy but Merrian (1956)[27] found irradiation to be of hardly any help Elliot (1954 and 1957)[28 & 29] claimed good results with continuous subconjunctival hydrocortisone therapy We subjected our cases of Eales's disease to varied forms of therapy and divided them into four groups (Table III)

A 25 mgms of subconjunctival hydrocortisone every two weeks —16 cases

B 25 mgm subconjunctival hydrocortisone every two weeks and 25 mgm androgen i m twice a week — 9 cases

C 25 mgm subconjunctival hydrocortisone every two weeks and choline and methionine on alternate days — 12 cases

D A combined therapy of 25 mgm of subconjunctival hydro cortisone every 2 weeks 25 mgm of androgen intramuscularly twice a week and of choline and methionine on alternate days—21 cases

The treatment was carried out for a period of 6 months to one year in every case and have been under observation for a period of 2 years or more

Our results show that in group A 4 out of the 16 cases treated showed a recurrence The series is comparable to the series of Elliot (1954)[28 29] and Agarwal et al (in press)

In group B there were recurrences in 2 out of the 9 cases treated and the results are almost the same as in group A Androgens do not seem to influence the results In group C there were recurrences in 2 out of the 12 cases treated and the results are superior to those of groups B and A The therapy in group C was instituted because of the positive history of liver disease in several of our cases and the know ledge that experimental choline deficiency can lead to retinal haemorr hages Even in tubercular haemorrhagic lesions of the retina choline has shown beneficial results due to its lipotropic and anti haemorrhagic action[30]

In group D there were recurrences in 2 out of 21 cases The group includes cases which had been previously treated either in group A or B or C and had shown the recurrence of the disease also From these results the combined therapy seems to be quite useful

Diathermic closure of bleeding vessels in perivasculitis has been put to practice with encouraging results[31 33]

Light coagulation[34] is now being utilised for the same purpose In twelve cases we utilised transcleral diathermy coagulation but

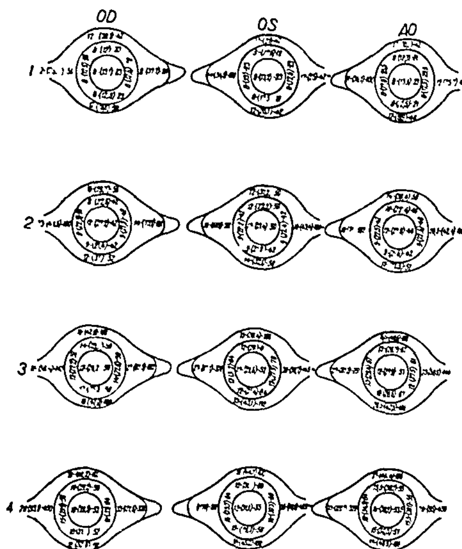


Fig. 1

Mean topographic esthesiograms of bulbar conjunctiva and cornea in mgr pressure in the right eye (O D) in the left eye (O S) with their general resultant in both eyes (A O) normal on the ground (1) and immediately after the return from the 5 000 m (2) 12 000 m (3) and 15 000 m (4) altitudes

rapid and marked in bulbar conjunctiva than in cornea — a parallelism evidently between groups, both within the sensibility of the same eye as between the right and the left eye

INTERPRETATION OF RESULTS

In our country, these two ocular sensibilities normally present the following characteristics

1 Bulbar conjunctival sensibility is comprised between 11 and 100 mg, the mean varying between 19,9 and 36,1 mg, and presents the seat of both thresholds in the nasal region

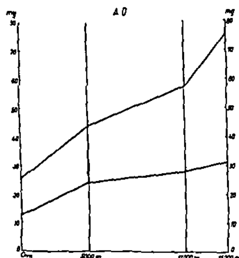


FIG 2

The resultant general mean of global sensibilities of bulbar conjunctiva (above) and of cornea (below) in mgr pressure in both eyes (A O) normal on the ground and immediately after the return from th 5 000 m 12 000 m and 15 000 m altitudes

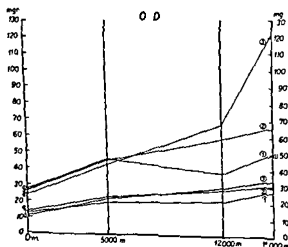


FIG 3a

Mean global sensibilities of bulbar conjunctiva (above) and of cornea (Fig 3b) in mgr pressure in the right eye (O D) and in the left eye (O S) normal on the ground and immediately after the return from the 5 000 m 12 000 m and 15 000 m altitudes in three identical category groups for both eyes (1) (2) (3) as against the same altitudes

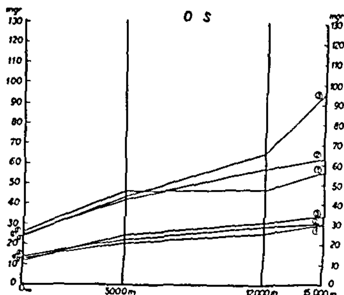


Fig 3b

2 The corneal sensibility is comprised between 8 and 25,5 mg the mean varying between 12,3 and 12,8 mg, and presents the seat of the nether threshold, identical on the entire surface of the cornea, and the seat of the upper threshold, identical in the nasal and temporal regions

Hence *it results that the bulbar conjunctival sensibility has its extreme thresholds concentrated only in the nasal region,* while *the corneal sensibility has its nether threshold diffused on the entire surface of the cornea,* and *the upper threshold in the nasal and temporal regions, where it is identical*

At altitudes of 5 000, 12 000 and 15 000 mm the extreme thresholds of both ocular sensibilities move their topographic seat in an orderless succession Thus it results that the local innervation factor — which could explain on the ground the topographic seat of thresholds — can now no longer justify the changed seat of sensibility thresholds, and that the appearance of a threshold in another region than in the one in which it existed on the ground or at the previous altitude, points out to the removal of previous sensibility limits at the setting up of a new state of sensibility

But, if the topographical thresholds of each ocular sensibility become partially modified, both sensibilities — considered in their general mean, a resultant of global sensibilities — return unmodified the normal ground, threshold relation of the general sensibility of bulbar conjunctiva, very much higher, as against that of the cornea They manifest an ascent proportional to the altitude from which they return, but more rapid and marked in bulbar conjunctiva than in cornea The threshold ascent of ocular sensibilities is manifest both for all cases in general, in both eyes taken together, and particularly for groups of cases, either in each eye considered separately or in comparison with the opposite eye, when an almost perfect concordance of sensibilities is noticed

Thus the altitude raises proportionally with its own level, the tactile sensation threshold of the two anatomo functional individualities of the ocular anterior hemisphere but within each individuality the tactile sensation modifies in a disorderly way its topographic distribution

CONCLUSIONS — THERAPEUTICAL SUGGESTIONS

The disorderly modifications of topographic thresholds within each of the two ocular sensibilities are due in the bulbar conjunctiva to vascular disturbances which occur in the arterial pressure of the cephalic segment and implicitly in the conjunctive region while in the cornea they are the consequence of the ophthalmotonus returned now to normal after it had previously decreased at high altitudes

The normal relation from the ground between the much higher general sensibility threshold of the bulbar conjunctive, as against the cornea, is being maintained and accentuated with the increased distance between them in proportion to the altitude from which they returned particularly because of the more rapid and marked ascent of the bulbar conjunctival threshold

This reduced sensibility comparable to the nervous lesion of a transitory anaesthetic type and with a *reduced trophesy* significance constitutes a favourable biological fund for any lesion infection or any other eventual pathological process the healing of which will be achieved slowlier if the pathological process sets in either immediately after landing or especially during the flight Hence the necessity that both in engaging and at the periodical controls of aviators both sensibilities be normal In any case it should be compulsory that before any conjunctival or corneal treatment an esthesiometrical examination of the aviator be carried out in order to investigate and have also in view the functional state of the subject under treatment

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OCULAR MANIFESTATIONS OF THE MECHANISM OF THE ACTION OF STRYCHNINE ON THE ORGANISM SET IN CONDITIONS OF HYPOBARISM AT HIGH ALTITUDES

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Previous, recent researches, both clinical, carried out at the Aviation Medical Center (7)(8)(9), and experimental, executed at our Institute (6), have shown that the eye constitutes a delicate indicator of modifications appearing in the functional equilibrium of the organism subjected to the action of high altitude hypobarism

Experimental researches (6) have emphasized the following principal modifications 1 *Mydriasis*, as a consequence both of the CO_2 accumulation, which excites the higher nervous centers (as evidence the fact that the pupil immediately reverts to normal if the barochamber is being ventilated, the atmospheric pressure being maintained unchanged), as well as of the algo irido motor reflex, induced by the painful mechanical excitation of the respective intero receptors, by the increased volume of gases which distend the viscera and the myelinic cover of the sensitive nerves, in proportion to the depression (as evidence the pupil reverting to normal, together with the re establishing of atmospheric pressure) The third, mydriatogenous mechanism is, undoubtedly, connected with the *anoxious* hyperadrenalinaemia described by Malmejac and Chardon (12), who have shown, on the one hand that *anoxaemia* induces the hyperactivity of the medullo suprarenal gland and the increase in adrenaline secretion, and on the other, the fact that the severing of the splanchnic nerves — i e the denervation of the suprarenal glands — stops the anoxious hyper adrenalinaemia, along the same line we may mention that Prof I I Nitescu has noticed the increased weight of the suprarenal capsules of the animal, after its being subjected to hypobarism In the state of maximal 9 mm mydriasis, which occurs at a 200 mm Hg depression, the photo irido motor reflex no longer appears, but it only occurs after a prolonged luminous excitation, in a medium 7 mm mydriasis, which had appeared at the 100–300 mm Hg depression, a fact which indicates the proportionally faintly differentiated rise in the threshold of this reflex alongside the atmospheric pressure 2 *The rapid chorio retinal arteriolar spasm, followed immediately by the established chorio retinal arteriolar dilatation accompanied by the respective venolar dilatation* the vascular spasm is the consequence of the suddenly and abnormally increased blood flow under the influence of hypoxia, indicating a vascular defence reflex reaction, while the vasodilatation is the con sequence of hypoxia itself — proof that, if the same altitude is main tained, it disappears on the ventilation of the barochamber — indicat ing a vascular decompensation phenomenon 3 *The diffuse retinal oedema in relatively circular zones, situated near the papilla,* is the

consequence of the derangement of certain endocular bio physico chemical mechanisms which locally modifying the normal osmotic exchanges, have induced the call of fluid into the retina, which in time, may constitute the starting point for an eventual detachment of the retina

4 *The aero embolism of the branches of the retinal vascular tree, and sometimes the orbital aero embolism* the former is the consequence of the liberation of gases dissolved in tissues in the form of gaseous bubbles dragged along by the circulatory stream, while the second is the consequence of the freeing of gases dissolved in the retroocular adipose tissue, in the form of diffu e gaseous infiltration of the orbital cellular tissue — orbital emphysema — with the consecutive protrusion of the eye and the sensation of crepitation at a slight pressure of the eyeball in the orbit

Knowing the behaviour of certain ocular components in connection with the general behaviour of the rabbit our research animal set in conditions of high altitude hypobarism we intended to establish whether and to what extent the same research animal set in similar experimental conditions but influenced by strychnine a drug with a central excitant action, studied by some of us in previous complex researches (1)(2)(3)(4), exhibits this time improved of aggravated general or ocular behaviours In the latter case, Cluzet, Piery, Ponthus, Mithaud (10) have shown that strychnine has often enabled animals to resist better to strong depressions and to attenuate or delay electro cariogramic modifications

Establishing the behaviour of the animal in these combined experimental conditions is of use in the first place for determining the mechanism of the action of strychnine in conditions of high altitude hypobarism and still more so for the eventual therapeutical suggestions which may offer valuable indications for aviation medecine

RESEARCH METHOD

The research was first carried out on the ground and then in the barochamber in order to appreciate correctly by comparison, the ocular manifestations of the organism strychninized and set in conditions of high altitude hypobarism as against ocular manifestations of the strychninized organism in conditions of normal atmospheric pressure

1 *The strychninization in conditions of normal atmospheric pressure*

The action of strychnine on the research animal (rabbit) has been performed (1) by direct (local) ocular and indirect (general) ocular contact

The direct (local) ocular contact has been practised either (though seldom) by *subconjunctival injections* or (almost always) by *mono or bilateral instillations* both on eyeballs with normal permeable, lachrymal ducts (permitting lachrymal draining by the normal ducts into the higher digestive duct) or rendered experimentally impervious (by the cauterization of palpebral lachrymal points 5 days before the

instillation, in order that, at the moment of the experiment, the painful mydriatic factor should have disappeared and the cicatrization finished, the variable factor of the lachrymal dilution has always been avoided by the absorption with filter paper of the tears present at the beginning of the experiment, which was carried out without immobilizing the animal or its head, and with the utmost gentleness, by soaking the filter paper in the lachrymal fluid at the bottom of the lower conjunctival *fornix conjunctivae*, rendered evident by the delicate traction downwards, by the thumb, of the lower lid, without touching the cornea or the conjunctiva, in other words, the tears were removed without fear or pain — both engendering mydriasis — for the animal

The indirect (general) contact has been practised either, though rarely, by *intravenous injections* or, almost always by *subdural mono or bilateral injections or by mono- or bilateral cortical application of filter paper washers or cottonwool pads imbibed with strychnine*

Researches were carried out both separately with each experimental type or by the consecutive and synchronal interference of all these, as for instance strychnine has been put in contact with the organism, simultaneously or at different times, either by its monocular instillation associated with its monocular cortical application on the opposite or on the same side of the instillation, or by its biocular instillation with its cortical mono or bilateral application, etc

We have thus studied the action of strychnine upon the tonicity of peri ocular, irian and corio retinal vascular musculature in albino rabbits

The study of the dynamics of peri ocular musculature has been carried out by the observation of the movements of the eyeball

The study of the dynamics of the musculature of the iris — has been executed by measuring the pupillary diameter after the contact of the organism with the respective drugs *Dynamic pupillometry*, i e *the measurements of the movements of the apparent pupillar diameter* — the real one being modified by the increased diopter cornea — aqueous humour — indicates in substance, objectively the irido kinesimetry, i e *the measurement of the dynamics of the musculature of the iris* Irido kinesimetry has been performed as follows in the animal placed on the observation table, always identically illuminated, with its eyes exposed to an invariable source of light, situated medianly at the extremity of its nose and from below upwards, the pupillar diameter was measured with a metallic blade, millimetrically graduated, superposed parallely to the pupillar plane, and as near as possible to the eye As the rabbit eye is oval, with a vertical great axis, we have always measured, for commodity sake, its horizontal diameter

In our researches we have tried to eliminate all factors of error which may modify the pupil, due to causes foreign to those of the action of the drug studied To this effect we have removed from the beginning the two factors of error — pain and fear — each partially inducing mydriasis, to this effect, after being taken out of its hutch,

the rabbit was not only not incommodated by any immobilization, but was left to calm down for 30 minutes on the observation table and for subsequent experimental necessities the animal was handled with the utmost calm and kindness The experiment was always carried out only on rabbits with normal pupillar diameters i e rigorously bilaterally exact in their horizontal diameter slightly inconstant variable around 5 mm and which reduced itself to 4 mm by the photo indo motor myosis incited by the 5 V Zeiss ophthalmoscope

The study of the dynamics of the musculature of corio retinal vessels in albino rabbits was carried out by ophthalmoscopic examination of the modifications of the vascular calibre

2 *The strychninization in conditions of high altitude hypobarism*

In some of the tests the rabbit was left free in the barochamber in order to observe its general behaviour as well as, at the same time and within possibilities the ocular one in general In other tests the rabbit was immobilized without fastening its head for the bilateral observation within possibilities of the movements of the eyeball and of the pupillar and corio retinal modifications In the third group of tests the rabbit was immobilized with the head fastened in flexion to the right or left resting on the transparent window of the baro chamber for observing the movements of the eyeball and measuring the modifications in the pupillary diameter, as well as to explore ophthalmoscopically the blood vessels in the eye fundus

The rabbit was then submitted with or without strychninization to very high ascents between 8 000 and 12 000 m corresponding to atmospheric pressures between 267 and 145 mm Hg The ascent to 8 000 m took 1 min 50 sec, and the return to the ground 37 sec the ascent to 9 000 m 2 min 5 sec and the return 40 sec, the ascent to 10 000 m 2 min 24 sec, and the return 44 sec the ascent to 11 000 m 2 min 40 sec and the return 48 sec and the ascent to 12 000 m 2 min 58 sec and the return to the ground 53 sec

The experimental prototype most often used has been the ascent to 9 000 m i e to 230 mm Hg atmospheric pressure with a 3 min exposure and a subsequent 3 min rest on the ground At one sitting the same animal was subjected up to ten ascents and in a period of one to three days in another 2–3 sittings to a total of 23 ascents

All strychninization techniques used on the ground achieving the same general and ocular effect — as seen below — the strychnini zation used during the fictitious ascents in the barochamber consisted in the direct ocular (local) contact of mono and bilateral strychnine instillations on the eyeballs with normal permeable lachrymal ducts

The study of the dynamics of musculatures peri ocular of the iris and of the chorio retinal blood vessels in albino rabbits has been carried out in conditions of investigation similar to those performed with strychnine on the ground We mention that *the study of the dynamics of the musculature of the iris* has been carried out in constant luminous conditions by

measuring the pupillary diameter with a metallic blade, millimetrically graduated, pressed to the window of the barochamber and superposed parallely to the horizontal pupillary plane The pupillary modifications, determined by the action of strychnine upon the rabbit in conditions of high altitude barochamber, have also been studied in connection with the photo-irido motor reflex

THE RESULT OF THE RESEARCHES

1° *Strychninization in conditions of normal atmospheric pressure*

1st Experiment 0,05–0,10 ml monocular subconjunctival injection or monocular instillation of 1–2 drops, both in 1% strychnine solution, induce after 1–6 min generalized tonic or tonico clonic convulsions, accompanied by disorderly and transient nystagmyformous jerks, intensive and generalized retinal arteriolar spasms and bilateral maximum mydriasis, which are usually followed by a state of sleepiness concommitantly with the disappearance of the phenomena described and the setting up of myosis, or often exitus N B the effect is more delayed in the case of instillations on the eyeball with experimentally impermealized lachrymal ducts, than on the eyeball with normal permeable lachrymal ducts

2nd Experiment The intravenous injection, the sub dural, mono or bilateral injection, both of 0,05–0,10 ml of a 1% strychnine solution, the cortical mono or bilateral application of filter paper washer or cottonwool wads, impregnated with a 1% strychnine solution, induce, after a few seconds, the same phenomena, followed almost always by exitus

3rd Experiment Ocular instillation or cortical application of a 1% strychnine solution to animals with the cortex previously brought into contact with a 10% chloral hydrate, have no effect or may induce, though very belatedly and very reducely, the general and ocular phenomena described above, mydriasis may be replaced by sleep myosis

2° *Strychninization in conditions of high altitude hypobarism*

Researches carried out in conditions of fictitious high altitude hypobarism in barochamber, without and with the mono and bilateral instillation of 1–2 drops of a 1% strychnine solution (for comparison purposes) yielded the following results

1 The general resistance of the animal decreases proportionally, on the one hand, to the ascent to heights of between 8 000 and 12 000 m, and, on the other, to the time of exposure at these heights Thus, dyspnea, rythmic pulsation of the head, cyanosis of the mucuous membrane of the nose, abdominal distension, mydriasis, chorio retinal vasodilatation set in ever clearer and more rapidly, the higher the ascent and the longer its action lasts, finally reaching exitus

in seven of these 12 cases there was recurrence and another vein in a different quadrant was found to be involved My learned colleagues to follow will throw more light on this problem

The aetiology of Eales's disease still eludes us and the therapy remains empirical and conjectural A combined therapy of hydrocortisone and methionine and choline does hold promise and is worthy of a trial The prognosis of the condition has shown some improvement during recent years but still remains gloomy

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2 The general resistance of the animal increases by the repetition in time of ascents — i e with training — and less by the time of exposure in these ascents The known phenomena present, this time, a delayed appearance and an attenuated manifestation

3 The general resistance of the animal is variably modified by previous strychnine instillations Thus, after the ascents supported with difficulty the strychnine instillations, *in a small dose* increases to such an extent the resistance of the untrained animal and all the more so that of the trained one that it can easily be ascended anew, but this time to a higher altitude than the one before, while the return to normal during the rest, at atmospheric pressure on the ground, occurs evidently more rapidly The high excitability threshold of the animal — contained between the upper limit, where no apparent effect is manifest and the lower limit reached sometimes and rendered evident by a slight mydriasis together with the state of slight general tremblings, occurring after slapping the animal slightly on the back with the palm — accompanies the increased resistance of the organism to ascents The strychnine instillation *in a large dose* inducing tonic and tonico clonic convulsions reduces the resistance of organism, both in trained and untrained animals even in connection with ascents which were easily supported before strychninization while the return to normal during the rest on the ground is much delayed or replaced by exitus the very reduced excitability threshold of the animal — contained between the upper limit where generalized convulsions disorderly and transient nystagmiformous jerks generalized retinal arteriolar pasms and intensive maximum bilateral mydriasis, that appear together in similar intensities and the lower limit reached by exitus — accompany the reduced resistance by the organism in ascents

The photo irido motor reflex is absent during the maximum mydriasis it is much delayed during medium mydriasis and only slightly delayed in the case of discreet mydriasis

INTERPRETATION OF RESEARCHES

I Strychninization in conditions of normal atmospheric pressure

It is therefore evident that the action of strychnine brought *into* contact directly ocularly or centrally manifests *itself in* both cases in the same manner as after the contact of strychnine with the cortex, by the intermediary of the same natural, chemical mediator, liberated subsequently and with a multiple effect upon the eye (1)

Instilled into the *fornix conjunctivae* of the O S, the strychnine is being resorbed either *slowly* only through the conjunctive if the experimental obstruction of the lachrymal ducts has been induced or *rapidly* by the normal lachrymal ducts oesophagus and stomach The resorbed strychnine passes in both cases into the sanguine circuit and reaches the higher nervous centres The *slow resorbtion* takes place by the higher conjunctivo angio nervous way, while the rapid resorbtion by the higher lachrymo-nasal digestive angio nervous

way. Whether the strychnine reaches, by these ways with an ocular starting point, the higher nervous centres, or is set directly into contact with these centres, it increases their reactivity towards the Ach, which stimulates the centres and induces, on the one hand, tonic or tonico-clonic convulsions and disorderly and transient nystagmy-formous jerks, by the neuro-muscular way, while, on the other hand, it stimulates the suprarenal capsule by the neuro-suprarenal way. Adrenaline actively freed and disseminated throughout the organism by the sanguine way, influences the heart with the vessels of the general circulation, among which also the ocular vascular tree, determining general and intensive arteriolar spasms, visible ophthalmoscopically, and maximum bilateral mydriasis by the suprarenal-angio-retino-irino way.

The histamine, produced in consequence of the increased exertion of the musculature submitted to alternations of muscular contractions and decontractions, manifested in the form of generalized convulsions, and in consequence of the increased work of the organs in general, impedes the higher nervous centres and leads to the state of torpour, which constitutes the state of histaminic shock, in the course of which the myosis also manifests itself.

An evidence that strychnine raises the reactivity of the higher nervous centres towards the Ach, which stimulates the centres and then unleashes the respective mechanisms and phenomena, is the fact that the chloral hydrate in a large dose with the "impeding action upon the nervous system towards the Ach", after Danielopolu (11) suppresses or at least admits a very tardy and reduced manifestation of the general and ocular phenomena which strychnine alone induces immediately and exaggeratedly.

2° The strychninization in conditions of high altitude hypobarism

The general resistance of the untrained and trained animal is evidently increased by strychnine instillations *in a small dose* which is non-convulsive, while, evidently, the general resistance is reduced by strychnine instillations *in a large dose*, which is convulsive.

In the first case we have a stimulation of the organism, while in the second an exhaustion of the organism leading to exitus.

Thus the action of strychnine depends upon the dose administered.

The ocular manifestations within the mechanism of the action of strychnine upon the animal set in conditions of high altitude hypobarism show, themselves, *the degree* by which strychnine increases the reactivity of the higher nervous centres towards the Ach, which stimulates the centres in the respective intensity, determining, on the one hand, *in a small dose* the rise in the general excitability threshold, contained between the higher level, where no phenomenon is apparent, and the lower limit, where a discreet mydriasis and a state of generalized slight tremblings set in, at the light tapping with the palm, on the back of the animal, and inducing, on the other hand, *in a large*

dose a very accentuated lowering of the general excitability threshold, contained between the higher limit, exhibiting the following phenomena which occur together in similar intensities tonic and tonico clonic convulsions with disorderly and transient nystagmyformous jerks generalized and intensive retinal arteriolar spasms and maximum bilateral mydriasis and the lower limit reached by exitus

Thus *in a small dose strychnine raises slightly* the reactivity of the higher nervous centres towards the Ach which stimulates these centres in the same degree and sometimes determines manifestations which indicate the reaching of the lower limit of the raised general excitability threshold In this case the stimulation of the higher nervous centres by the Ach in consequence of the increase in the reactivity of the centres towards the Ach under the influence of the small dose of strychnine induces by the three following ways the manifestations described above namely by *the neuro muscular way* the state of delicate generalized tremblings at the slight superadded excitation of a light tapping with the palm on the back of the animal by *the neuro suprarenal way* the slight stimulation of the suprarenal capsule *by the suprarenal angio irian way* the discreet state of bilateral adrenalinic mydriasis by the slight increase in the irido dilatating tonus and the slight decrease in the irido constrictor tonus

In a large dose however *strychnine raises exaggeratedly* the reactivity of the higher nervous centres towards the Ach which stimulates similarly these centres and induces phenomena which indicate the very marked decrease in the general excitability threshold In this case the stimulation of the higher nervous centres by Ach in consequence of the increase in the reactivity of these centres towards the Ach under the influence of the large dose of strychnine, induces by the following three ways the above described manifestations namely *by the neuro muscular way* the state of tonic and *tonico clonic convul*sions accompanied by disorderly and transient nystagmyformous jerks *by the neuro suprarenal way* the strong excitation of the suprarenal capsule *by the suprareno angio retino irian way* generalized and intensive retinal arteriolar spasms accompanied by maximum bilateral adrenalinic mydriasis following the great increase in the irido dilatating tonus and the great decrease in the irido constrictor tonus

In a small dose therefore with a weak action strychnine yields similar effects to those of any other central stimulant of any nature (psychic physical chemical) but with the same slight intensity of action which raises the general excitability threshold between a higher limit, where there is no apparent phenomenon and a lower limit where a discreet mydriasis and eventually a light state of general hyperexcitability set in

In this respect in the researches of some of us (5) it was shown for instance that in the case of glaucoma in which a psychic factor is acting and thus with a central action this increases *slightly* the reactivity of the higher nervous centres towards the Ach which stimulates *slightly* the higher nervous centre *and stimulate most discreetly*

the suprarenal capsule, while *the actively liberated adrenaline in a very small quantity* and spread throughout the organism by the sanguine way, accompanied by a local ocular factor, with a propensity to glaucoma, determines the *glaucomatous mydriasis*

The fact that the adrenaline enters the physiopathological circuit of the glaucoma has been demonstrated by Popov (quoted at (13)) who, analysing the blood of the glaucomatous patients, has discovered in most of them an increase in Ca and Adr, accompanied by a decrease in K,I and choline In the same sense, Platneva, Raeva and Voronina (quoted at (13))—examining, by the Levi method, the aqueous humour of glaucomatous persons, have brought to light the presence of the adrenalinic sympaticotropous chemical mediator, which raises the activity of the heart and much more seldom that of the vagotropeous substance, the acetylcholine, which diminishes the activity of the heart, a proof of the disturbance of the sympathetic parasympathetic equilibrium of the nervous vegetative system in the glaucoma, with a sympathetic predominance

These facts constitute yet another argument in favour of mydriatogenous adrenalinic mechanism, generally a consequence of any central excitant, their different action intensities explains the degree of the mydriatic manifestation, in the sense that the discreet mydriasis is the consequence of any weak central excitant, such as for instance strychnine in a small dose, while maximum mydriasis is the consequence of any powerful central excitant, such as strychnine in a large dose

The degree of *spontaneous* adrenalinic mydriasis shows the directly proportional intensity of the degree of excitation of the higher nervous centres and, at the same time, on this background, the absence or the great or discreet latency of the photo irido motor reflex is to be explained

CONCLUSIONS

Practical therapeutical suggestions for aviation medecine

In *a large dose*, *strychnine*, administered in conditions of high altitude hypobarism, excites the higher nervous centres to the extent that the predominance of central phenomena, which *can no longer be compensated by the defence mechanisms of the organism*, leads to exhaustion and exitus *In a small dose, strychnine* administered in similar conditions of high altitude hypobarism, excites the higher nervous centres to the extent that *it stimulates the defence mechanisms of the organism*, among which, within the fight of the organism against anoxaemia, a paramount role is occupied, particularly by the hyperfunction of the medullo suprarenal

These experimental data suggest that the general adaptation capacity of high altitude aviators may be increased during the flight by the administration of small doses of strychnine

The Laboratory for Clinical and Experimental Physiology and Physiopathology of the Eye of the Normal and Pathological Physiology Institute 'Daniel Danielopolu' of the Academy of the Roumanian

People s Republic Director of the Institute Academician Prof Dr Gr Benetato

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LES TROUBLES VISUELS ET LEURS CONSEQUENCES SUR L ORGANISME DANS LES CONDITIONS DE PERCEPTION AU DISPOSITIF RADAR

par

M CARAPANCEA M POPESCO M STEFAN

(*Roumania*)

METHODE DE RECHERCHE

Toutes les recherches cliniques effectuees sur une echelle internationale ont unanimement démontre que les radiations du radar ne justifient pas les troubles visuels et generaux associes du personnel qui travaille dans ces conditions

Nos investigations ont tout d abord precise les conditions complexes du travail de l appareil visuel au radar et a ses annexes complementaires liees a la duree du travail visuel la distance a laquelle s effectue ce travail visuel et la luminosite des ecrans Après cela nous avons poursuivi avant et comparativement apres la fin du travail visuel, les suivants objectifs l acuite visuelle la refraction à la skiascopie, la proximometrie avec le proximometre M Carapancea

the suprarenal capsule, while *the actively liberated adrenaline in a very small quantity* and spread throughout the organism by the sanguine way, accompanied by a local ocular factor, with a propensity to glaucoma, determines the *glaucomatous mydriasis*

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In *a large dose, strychnine*, administered in conditions of high altitude hypobarism, excites the higher nervous centres to the extent that the predominance of central phenomena, which *can no longer be compensated by the defence mechanisms of the organism*, leads to exhaustion and exitus *In a small dose, strychnine*, administered in similar conditions of high altitude hypobarism, excites the higher nervous centres to the extent that *it stimulates the defence mechanisms of the organism*, among which, within the fight of the organism against anoxoemia, a paramount role is occupied, particularly, by the hyperfunction of the medullo suprarenal

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generale variant entre 8 et 14 mg et un esthesiogramme de la con jonctive bulbaire a moyenne variant entre 11 et 23 mg c est a dire — vis a vis de nos recherches anterieures d esthesiometrie, effectuees au sol de notre pays (1) — avec les seuls superieurs de ces sensibilites, moderement baisses a la cornee et tres accentues a la conjonctive bulbaire, ce qui indique une legere augmentation de la sensibilite corneenne et une tres accentuee augmentation de la sensibilite de la conjonctive bulbaire (Fig 1)

La repartition du pigment retinien maculaire et perimaculaire a rarement presente des deficiences et surtout chez les hypermetropes

Les recherches effectuees ont rendu evidente *l identite des troubles visuels et generaux associes chez tous les hypermetropes des deux premiers groupes à acuite plus accentuee dans le premier groupe comparé au second et l absence presque complete des m emes phenomenes au troisieme groupe, temoin*

Donc *seulement les hypermetropes mis dans l etat de sur sollicitation visuelle* manifestent avec le temps — soit dans un bref delai ou bien plus tard apres des mois de travail visuel et *specialement* en fonction des periodes plus soutenues de travail — toute une serie de symptomes subjectifs et objectifs oculaires et generaux associes qui une fois installes se *manifestent* continuellement au courant de la vie journa liere a l occasion de toute sollicitation de la vue

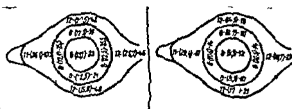


Fig 1

Esthes ogrammes topographiques moyens de la cornee et de la conjonctive bulbaire en mg press on presentés sous forme de resultante générale pour les deux yeux. À gauche chez le normal ( ) A droite chez les hypermetropes qui travaillent soit au radar soit aux planchettes horizontales de près et verticales de distance

(1) Carapancea M Popesco M Ratiu E Pintilie I Stoian M Stefan M La sensibil te de la conjonctive bulbaire *et* de la cornee dans des *conditions* d hypobarisme chez les pilotes de grande altitude Communication presentee a l *Inst tut de Physiologie Normale et Pathologique D Da ielopolu ue l Academie de la Republique Populaire Roumaine* dans la seance du 15 XII 1960 sous la présidence du Directeur de l Institut l Academic en Prof Dr Gr Benetato

( ) Carapancea M Popesco M Ratiu E Pintilie I Stoian M Stefan M La sensibilite de la conjonctive bulbaire *et* de la cornee dans des conditions d hypobarisme chez les p lotes de grande altitude. Communication presentee a l *I stit t de Physiolog e N male et Patholog que D D r ielopolu de l Academie de la Rep bl que Populaire Roumaine* dans la séance du 15 XII 1960 sous la présidence du D recteur de l Inst tut l Academ cien Prof Dr Gr Benetato

et M Popesco (1) et l'esthesiometrie corneenne et conjonctivale bulbaire avec l'esthesiometre L Ratiu et A Ivanovici (2)

Simultanement on a aussi examine le fond de l'oeil pour determiner la repartition du *pigment* retinien maculaire et perimaculaire

Ces recherches ont ete effectuees sur 107 travailleurs des stations de radiolocation, *ages de 19 a 33 ans, repartis* en trois groupes le premier groupe *forme d'operateurs* de radar, le second groupe d'enregistreurs et *lecteurs aux planchettes horizontales, de* pres et verticales, de distance, et le troisieme groupe de *radiotelegraphistes* et electromecaniciens, *etait en meme temps* le groupe temoin vis a vis des deux autres

RESULTATS DES RECHERCHES

Le *premier groupe* etait constitue *de 59 operateurs* de radar, dont 38 hypermetropes, 9 *myopes et* 12 emmetropes

Le second groupe forme de 22 enregistreurs ou lecteurs aux planchettes horizontales, de pres et aux planchettes verticales, de distance, comprenait 12 hypermetropes et 10 emmetropes

Le troisieme groupe — temoin vis a vis des deux autres — forme de 26 radiotelegraphistes et electromecaniciens — etait constitue de 18 hypermetropes, 2 myopes et 6 emmetropes

Les *hypermetropes* avaient *une* acuite visuelle comprise entre 1 et 1, 5, a refraction jusqu' a + 2 d et − 3 d Les myopes avaient une acuite visuelle comprise entre 1/1, 5 et 1/2, a refraction jusqu'a 1 d et −2 d

La proximometrie, comprise entre 9 et 14 cm, a enregistre, *seulement chez les* hypermetropes des deux *premiers groupes*—proportionnellement a l'age, l'acuite et la refraction de chaque cas considere individuellement—un leger rapprochement du punctum proximum

Le mesurage de la sensibilite corneenne et conjonctivale bulbaire a determine aux deux yeux et seulement chez les hypermetropes des deux premiers groupes, un esthesiogramme cornéen a moyenne

(1) Carapancea M Popesco M Pintilie I Stoian M Teodorescu V Stefan M Les modifications de l accommodation visuelle dans des conditions d hypobarisme chez les pilotes de grande altitude Communication presentee à l *Institut de Physiologie Normale et Pathologique D Danielopolu de l Academie de Republique Populaire Roumaine dans* la séance du *14 X 1960* sous la presidence du Directeur de l Institut l Academicien Prof Dr Gr Benetato

(2) Carapancea M Popesco M Ratiu E Pintilie I Stoian M Stefan M La sensibilité de la conjonctive bulbaire et de la cornee dans des conditions d hypobarisme *chez les pilotes de grande* altitude Communication presentee a l *Institut de Physiologie Normale et Pathologique D Danielopolu de l Academie de la Republique Populaire Roumaine* dans la seance du 15 XII 1960 sous la présidence du Directeur de l Institut l Academicien *Prof Dr* Gr Benetato

"mal visuel de train" mal visuel d'automobile, mal visuel de fiacre", (c) soit pour suivre le va et vient de la foule dans la rue, avec la sensation de peur des espaces pleins de foule" cirque, etc — sorte d' "agoraphobie visuelle" — avec la préférence des rues moins peuplées ou même désertes (3)

10 *Myodesopsie*

11 Photophobie légère au commencement et tenace plus tard

12 Crampes oculaires douloureuses

13 Myalgie légère des droits internes aux mouvements des globes dans l'orbite, à l'occasion de leurs sollicitation l'un après l'autre ou ensemble (3)

14 Douleurs oculaires aux mouvements des globes dans l'orbite (3) (5)

15 Douleurs rétro-oculaires (2) (3)

16 Sensation de fatigue palpébrale et oculaire (3) (5)

17 Préférence de garder fréquemment les paupières fermées pour *se reposer la vue*

18 Nécessité d'appuyer sur les yeux avec les doigts chauffés rapidement à une source proche de chaleur bec, fourneau, calorifère, etc (3)

19 Diplopie passagère *sans rémission pendant toute la vie*, qui apparaît soit au réveil, surtout le matin, comme "diplopie de bonjour", soit au courant de la journée, en des durées variant de quelques secondes jusqu'à quelques minutes et cessant généralement après un effort de fixation de l'image apparue double (3)

20 Parfois Migraine ophtalmique atypique, fugitive, manifestée par des hémianopsies homonymes partielles des scotomes scintillants atypiques et des céphalées instables en fait de moment d'apparition, *durée et siège* (3)

21 Parfois Sensation de tension intra orbitaire passagère

22 Parfois Adaptation diurne retardée de 10–15–30 minutes après la sortie de la chambre obscure du radar (3)

23 Parfois Photophobie à la lumière du jour et de la chambre (3)

24 Parfois Adaptation nocturne déficitaire par perception confuse continuelle à la lumière de nuit (3)

GÉNÉRAUX

1 Maux de tête passagers (3)

2 Douleur frontale en barre (1) (2) (3)

3 Douleur aux tempes (3)

4 Céphalée occipitale (3)

5 Céphalée diffuse tenace, d'habitude au courant de la deuxième moitié de la journée ou à la fin de la journée du travail visuel (1) (3) (5)

Ces symptômes au nombre de 59 — dont une part fut décrite aux radaristes par Berest, Gibert, Perdriel (1), Berest, Perdriel, Colin (2), Indeikin (4), Visnevski, Petrenko (5), et auxquels j'ajoute les symptômes inédits observés personnellement avec mes collaborateurs Popesco, Stefan, Bengulesco, Musetesco (3) — je les présente dans une systématisation personnelle, selon leur gravité croissante

Symptomatologie des troubles oculaires et généraux associés
Symptômes subjectifs
Oculaires

1 Sensation de démangeaison conjonctivale passagère (3)

2 Sensations de cuisson et de brûlure conjonctivale, passagères (1) (3)

3 Larmoiement passager (1) (2) (3) (5)

4 Sensation de piqûres intra oculaires passagères (1) (2) (3) (5)

5 Sensation de tension intra oculaire passagère (1) (2) (3)

6 Effacement passager de l'image vue comme à travers un brouillard fugitif (3)

7 Aperception visuelle fugitive (3)

8 Instabilité de la vision claire de près, passagère au début et accentuée, plus tard, pour lire, dessiner et, en général, suivre tous les détails rapprochés (3)

9 Instabilité de la vision claire de loin, passagère, au début et accentuée, plus tard (*a*) soit pour suivre les images au cinématographe, à la télévision, au théâtre, en amphithéâtre, en classe, etc, avec la préférence de rester au fond de ces différentes pièces, (*b*) soit pour suivre le défilé rapide des maisons, des arbres, des poteaux télégraphiques, etc, vus d'un véhicule en marche, avec les sensations de "mal visuel du passager pendant le décollage et l'atterrissage",

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GENERAUX

1 Vomis ements (3)

2 Parfois Facies de nevro e asthenopique, hypermetropique — instale a la longue et plus evident pendant l acte de regarder de pres-au suivantes particularites (a) sourcils abaisses à pli vertical du tegument inter sourcilier avec des douleurs consecutives sur sourcilieres (b) face legerement contractee ou meme crispee, avec l aspect concentre du visage (c) myosis avec l aspect severe du regard

3 Parfois Spasmes faciaux legers, divers, accompagnant les tics blepharo spastiques

4 Parfois Troubles inconstants du rythme cardiaque

5 Parfois — Titubation

N B Si tous les symptomes ci dessus ne se reproduisent pas toujours on y trouve au moins, toujours 90% de ceux ci

Independamment de l etat de refraction, nous avons constate parfois et seulement chez les operateurs de radar la diminution de leur capacite sexuelle

INTERPRETATION DES RECHERCHES

Les troubles polymorphes decrits tant dans la fonction de l appareil visuel que dans le fonctionnement de tout l organisme n apparaissent pas seulement comme des manifestations inexplicables, mais aussi sans liaison aucune entre elles

En realité l explication de ce polymorphisme symptomatique prend son point de depart dans la continuelle activite de l appareil visuel hypermetropique qui pour n importe quelle distance doit toujours former mathématiquement l image claire sur la rétine

Ce complexe travail, de mise à point continuelle de l image et qui constitue au fond l aboutissant visuel de tous les mecanismes oculaires explique la symptomatologie oculaire qui s y rattache

C est ainsi que l on peut expliquer en detail tous les symptomes mentionnes

— La sensation de demangeaison conjonctivale passagere

— Les sensations de cuisson et de brulure conjonctivale, passageres

— L augmentation esthesiométrique legere de la sensibilite corneenne et très accentuee de la sensibilite conjonctivale bulbaire,

Tous ces symptomes sont dus au fait qu au cours de l accommodation pour la vision de pres lorsque la frequence du clignement decroit et la circulation palpebro conjonctivale ralentit, il apparait une microstase tant palpebrale à oedème consecutif qu aussi conjonctivale d ou la pression exercee par cette microstase sanguine sur les terminaisons nerveuses locales palpebrales et conjonctivales determinent les phenomènes plus haut decrits

— La congestion passagère de la conjonctive palpebrale est un stade plus avance de la microstase sanguine décrite

6 États migraineux non définis (3)

7 État de malaise (3)

8 Vertige d'origine visuelle, passager au commencement et tenace *plus tard* (1) (3)

9 Hemicranie, du cote de l oeil directeur, soit sur un meme fond hypermetropique bilateral, soit sur un fond anisometropique

10 Inapetence (3)

11 Nausee discrete au commencement et tenace plus tard (3)

12 *Somnolence* continuelle et besoin imperieux de dormir apres quelques heures de travail visuel (3)

13 Fatigue generale (3) (5)

14 Complexe d'infeniorite par incapacite de devisager son interlocuteur, parce que cela provoque " un larmoiement intense " et " une douleur oculaire "

15 États asthenico depressifs (3)

16 États d inquiétude

17 États d'irascibilite (3)

Symptomes objectifs
Oculaires

1 Augmentation esthesiometrique legere de la sensibilite corneenne et tres accentuee de la sensibilite conjonctivale bulbaire (3)

2 Congestion passagere de la conjonctive palpebrale

3 Hyperemie conjonctivale bulbaire, accentuee par le sommeil et amelioree apres deux a trois heures de veille (2) (3) (5)

4 Ectasie des vaisseaux de la conjonctive bulbaire (3)

5 Conjonctivite papillaire

6 Conjonctivites frustes guerissant spontanément, au début et a caractere trainant et rebelle, plus tard, aux traitements habituels (3)

7 Congestion légere et fin oedeme du bord palpebral (1) (3)

8 Blepharo conjonctivite a predisposition aux folliculites ciliaires, orgelets et abces palpebraux (1) (3) (4) (5)

9 Rapprochement du punctum proximum (2) (3)

10 Parfois Troubles discrets dans la disposition du pigment retinien des regions maculaire et perimaculaire (3)

11 Parfois Hypertension retinienne provoquee ou aggravee en cas de préexistence

12 Parfois Tic blefaro spastique

13 Parfois Exophtalmie mono laterale, a peine esquissee et tres passagere

La contraction de l accommodation pour la vision de loin est peu accentuee et se passe lentement en 0 50 jusqu a 1 16 La contraction de l accommodation pour la vision de pres est maximale et se passe rapidement en 0 39 jusqu à 0 82 etant en meme temps accompagnee encore par deux autres reflexes de l appareil visuel le reflexe de la convergence et le reflexe du myosis

Il en resulte que comparee avec la vision de loin *la vision de pres est plus fatiguante puisqu elle necessite un mecanisme plus complique,* base sur trois reflexes intimement lies entre eux, a savoir le reflexe de l accommodation pour la vision de pres, le reflexe du myosis et le reflexe de la convergence Cependant le reflexe de l accommodation pour la vision de pres et le reflexe du myosis sont nullement synchrones et le réflexe de l accommodation pour la vision de pres et le reflexe de la convergence gardent chacun sa parfaite individualite puisqu on peut accommoder pour le regard de pres sans converger Mais le réflexe du myosis s installe presque synchroniquement avec le reflexe de la convergence puisque le myosis constitue la *syncinesie synergique innee* liee corticalement ou sous corticalement à la convergence des axes visuelles a partir déja du quatrieme mois

Le mecanisme de la vue claire, pour la vision de pres aussi bien que de loin provoque donc

1 Des efforts accommodatifs continuels qui conduisent à des contractions toniques et tres rarement cloniques du muscle ciliaire avec images tantot confuses tantot claires, se succedant lentement ou rapidement Autrement dit il se forme un etat d asthenopie accommodative d incapacite de perception soutenue par suite de la fatigue du muscle ciliaire continuellement sur sollicité

Une tres importante mention s impose a etre faite comparativement entre l hypermetropie et l astigmatisme tant hypermetropique simple et compose, que mixte Celle ci parce que *l hypercontraction uniforme* du muscle ciliaire sur tout le pourtour de sa surface qui se passe dans l hypermétropie, est bien sûr moins fatiguante *que l hyper contraction non uniforme parcellaire* seulement d une seule portion musculaire sur le fond de contraction generale de tout le muscle ciliaire tel que dans l astigmatisme hypermétropique simple et composé *l unique hypercontraction segmentaire* qui se produit dans l astigmatisme mixte apparait donc de ce fait comme moins fatiguante que celle des deux varietes d astigmatisme hypermetropique

Il resulte donc de ces raisons physiologiques que l astigmatisme hypermétropique simple ou compose fatigue l oeil de plus que l hyper metropie simple et que l astigmatisme mixte fatigue l oeil moins que l hypermetropie simple

2 Des contractions iriennes un reflexe de myosis pour la vision de près et un reflexe de retour a la normale parfois meme une légère mydriase pour la vision de loin

3 Des contractions de la musculature oculaire extrinsèque reflexe de convergence pour la vision de près reflexe de relachement

— *L'hyperémie conjonctivale bulbaire*, accentuée par le sommeil et améliorée après deux à trois heures de veille,

— *L'ectasie des vaisseaux de la conjonctive bulbaire*,

Ces deux symptômes sont dus au fait que la stase des vaisseaux conjonctivaux *est accentuée pendant le sommeil, tant par le ralentissement* de la circulation locale que par la chaleur des paupières qui recouvrent l'oeil, la stase s'améliore après quelques heures de veille, c'est-à-dire de reprise de la circulation sanguine et de contact avec l'air ambiant plus frais, cependant la stase ne disparaît pas complètement à cause de la reprise de l'acte accommodatif pour la vision de près à fréquence réduite du clignement, d'où cercle fonctionnel vicieux de la circulation locale, qui, avec le temps réalise la microectasie vasculaire irréversible, donc à conjonctives définitivement congestionnées

— La conjonctivite papillaire,

— Les conjonctivites frustes guérissant spontanément au début et à caractère traînant et rebelle plus tard aux traitements habituels,

— La congestion légère et le fin oedème du bord palpébral,

— La blépharo conjonctivite, à prédisposition aux folliculites ciliaires, orgelets et abcès palpébraux,

Ces symptômes sont dus au fait que la stase des vaisseaux conjonctivaux et palpébraux diminue petit à petit la résistance locale envers le microbisme latent — normalement présent — qui de la sorte, en fin de compte, peut exalter sa virulence d'où apparition d'infections de la conjonctive et ensuite du bord palpébral, au début à guérison spontanée et plus tard à caractère définitif et rebelle aux traitements habituels

— *Le larmoiement passager* est dû au réflexe à point de départ (*a*) soit de l'irritation cornéeo conjonctivale provoquée par leurs léger séchage, consécutivement à la fréquence réduite du clignement au cours de l'accommodation soutenue pour la vision de près, (*b*) soit de l'irritation blépharo conjonctivale inflammatoire, consécutivement à la stase des vaisseaux conjonctivaux et palpébraux (*c*) soit de l'irritation cornéeo conjonctivale conjointement à celle blépharo conjonctivale

* * *

Afin de mieux comprendre la physio pathologie des symptômes qui suivent et qui découlent de l'état fonctionnel du muscle ciliaire, l'élément principal de la vue claire, les suivantes constatations s'imposent dans le cadre de l'accommodation hypermétropique

Chez l'hypermétrope, le muscle ciliaire est sur-sollicité par l'activité accommodative, effort qui lui est imposé sans relâche, tant pour n'importe quelle vision de loin et même pour la vue à l'infini, puisque le punctum remotum est virtuel et situé au delà de l'infini, que surtout pour la vision de près, puisque le punctum proximum est situé derrière la rétine

visuel soutenu de près ainsi qu'en des phénomènes généraux à savoir céphalée vertige somnolence nausée, vomissements, troubles inconstant du rythme cardiaque

A part la conjonctivite aiguë que j'ai guérie en quelques jours je n'ai découvert aucun signe objectif pouvant justifier les troubles généraux dont il se plaignait

Plus tard j'ai eu à ajouter encore à cette observation les trois faits suivants

1 Les troubles généraux s'installaient d'habitude alors qu'il avait rapidement démonté graissé et rassemblé les parties de diverses armes, exercice continuellement répété en vue d'un examen d'armurier militaire

2 Les troubles généraux ont disparu pendant quelques jours après les injections intra-orbitaires mais pendant ce temps la vue se voilait toutes les fois qu'il faisait des efforts visuels à l'*occasion* des exercices pour son futur examen

3 Ce soldat guéri de la conjonctivite avec laquelle il s'était présenté et chargé de copier des situations sanitaires, se plaignit de *nouveau* après deux heures de travail des mêmes troubles généraux violents qui étaient mentionnés dans sa fiche médicale

Bien entendu que je n'ai aucunement pensé alors à une *relation* entre ces phénomènes généraux et son acuité visuelle *hypernormale de* 1 25 et son hypermétropie de + 2 d sph

Ces trois concours de circonstances qui m'ont paru bizarres à *l'époque deviennent* maintenant parfaitement explicables grâce à la *connaissance* des relations anatomo physiologiques d'entre l'*activité visuelle hypermétropique* et l'excitation du ganglion ciliaire à savoir

1 Les troubles généraux c'est à dire les *manifestations* pathologiques *viscérale* dépendaient de *excitations venant* du ganglion ciliaire étant en réalité des *reflexes cilio viscéraux* qui apparaissaient à la suite d'efforts prolongés de la vision de près

2 L'anesthésie bilatérale des ganglions ciliaires a interrompu les reflexes cilio viscéraux *puisque le* ganglion ciliaire était mis en impossibilité de *transmettre ces* impulsions anormales Pour cette raison et pendant toute la durée de l'*anesthésie* des ganglions ciliaires, les organes respectifs *ont repris* leur physiologie normale En *même* temps la vue se *troublait toutes les fois* qu'on faisait des efforts *visuels* de près prolongés le *muscle ciliaire* se fatiguant immuablement

3 L'*effet* de l'anesthésie bilatérale des ganglions ciliaires disparaissant et la voie des *reflexe* cilio viscéraux *se rétablissant* l'excitation des ganglions ciliaires *pendant* l'activité visuelle *et spécialement* pour le travail de *près a provoqué* de nouveau les troubles viscéraux liés anatomo *fonctionnellement au ganglion ciliaire*

Mais en dehors des reflexes *cilio viscéraux manifestes* sous l'aspect *des troubles* généraux décrits l'excitation du *ganglion ciliaire* provoque encore d'*autres* troubles généraux dus cette fois ci à l'*excitation* du

de la convergence pour la vision de loin et des alternances de contractions-relâchements de la musculature péri-oculaire striée à l'occasion des excursions des yeux.

Ces trois activités musculaires, exagérées chez l'hypermétrope, déterminent des impulsions nerveuses anormales, qui se transmettent par les filets nerveux respectifs, tant de l'intérieur que de l'extérieur du globe, à *la zone réflexogène orbitaire*, qui est *le ganglion ciliaire* (1).

Des recherches expérimentales de l'un d'entre nous ont démontré que les réflexes intéressant *divers organes* à point de départ oculaire, partent en réalité du ganglion ciliaire, c'est pourquoi on les appelle réflexes cilio-viscéraux (1) (2).

La définition de chaque réflexe cilio-viscéral (vasculaire, respiratoire, oesophagien, gastrique, intestinal, colique, vésical, glycémique et viscéro-moteur en général) comprend l'ensemble des troubles de l'organe respectif consécutifs à l'excitation exercée par le ganglion ciliaire.

Ces réflexes, manifestés donc sous l'aspect de troubles généraux à caractère polymorphe, incompréhensible et non liés entre eux, peuvent être expliqués uniquement par l'activité visuelle hypermétropique, qui excitant le ganglion ciliaire engendre les réflexes, plus ou moins forts, des viscères qui en dépendent.

A l'appui de ce point de vue, je cite, parmi les observations cliniques personnelles, le résumé de celle qui apparaît la plus impressionnante, vu qu'elle contient aussi les éléments fortuits d'une expérience évidemment démonstrative (3).

Au mois de novembre 1944 — époque où certaines unités militaires venaient de fusionner — il s'est présenté, à l'infirmerie de l'unité où j'étais mobilisé, un soldat, d'une autre unité, auquel — d'après les données notées dans sa fiche médicale — on avait novocaïnisé bilatéralement les ganglions ciliaires pour un glaucome aigu bilatéral.

Les manifestations du présumé glaucome — diagnostiqué et traité par un non spécialiste — consistaient en des phénomènes oculaires, à savoir : congestion conjonctivale aiguë bilatérale, mais exsudative, avec photophobie et vue trouble intermittente au travail

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visuel soutenu de près ainsi qu'en des phénomènes généraux à savoir céphalée, vertige, somnolence, nausée, vomissements, troubles inconstants du rythme cardiaque.

À part la conjonctivite aiguë que j'ai guérie en quelques jours, je n'ai découvert aucun signe objectif pouvant justifier les troubles généraux dont il se plaignait.

Plus tard j'ai eu à ajouter encore à cette observation les trois faits suivants :

1. Les troubles généraux s'installaient d'habitude alors qu'il avait rapidement démonté, graissé et rassemblé les parties de diverses armes, exercice continuellement répété en vue d'un examen d'armurier militaire.

2. Les troubles généraux ont disparu pendant quelques jours après les injections intra-orbitaires, mais pendant ce temps la vue se voilait toutes les fois qu'il faisait des efforts visuels à l'occasion des exercices pour son futur examen.

3. Ce soldat guéri de la conjonctivite avec laquelle il s'était présenté et chargé de copier des situations sanitaires se plaignit de nouveau après deux heures de travail des mêmes troubles généraux violents qui étaient mentionnés dans sa fiche médicale.

Bien entendu que je n'ai aucunement pensé alors à une relation entre ses phénomènes généraux et son acuité visuelle hypernormale de 1,25 et son hypermétropie de + 2 d. sph.

Ces trois concours de circonstances qui m'ont paru bizarres à l'époque deviennent maintenant parfaitement explicables, grâce à la connaissance des relations anatomo-physiologiques d'entre l'activité visuelle hypermétropique et l'excitation du ganglion ciliaire, à savoir :

1. Les troubles généraux, c'est-à-dire les manifestations pathologiques viscérales dépendaient des excitations venant du ganglion ciliaire, étant en réalité des reflexes cilio-viscéraux qui apparaissaient à la suite d'efforts prolongés de la vision de près.

2. L'anesthésie bilatérale des ganglions ciliaires a interrompu les reflexes cilio-viscéraux, puisque le ganglion ciliaire était mis en impossibilité de transmettre ces impulsions anormales. Pour cette raison et pendant toute la durée de l'anesthésie des ganglions ciliaires les organes respectifs ont repris leur physiologie normale. En même temps la vue se troublait toutes les fois qu'on faisait des efforts visuels de près prolongés, le muscle ciliaire se fatiguant immuablement.

3. L'effet de l'anesthésie bilatérale des ganglions ciliaires disparaissant et la voie des reflexes cilio-viscéraux se rétablissant, l'excitation des ganglions ciliaires pendant l'activité visuelle et spécialement pour le travail de près a provoqué de nouveau les troubles viscéraux liés anatomo-fonctionnellement au ganglion ciliaire.

Mais en dehors des reflexes cilio-viscéraux manifestés sous l'aspect des troubles généraux décrits, l'excitation du ganglion ciliaire provoque encore d'autres troubles généraux dus cette fois-ci à l'excitation du

cortex cérébral, soit directement par voie cilio-corticale, soit indirectement par toutes les voies reliant au cortex les viscères sujets aux troubles cilio-viscéraux. Ce genre de troubles généraux ne sont donc autre chose que l'effet des excitations corticales dues aux réflexes cilio-corticaux et au reflet cortical de retour des réflexes cilio-viscéraux.

* * *

Les considérations ci-dessus nous permettent de mieux comprendre la physio-pathologie des symptômes qui suivent, et qui découlent de l'état fonctionnel du muscle ciliaire, dans le cadre de l'accommodation hypermétropique :

— La sensation de piqûres intra-oculaires passagères,

— La sensation de tension intra-oculaire passagère,

Les deux symptômes sont dus aux contractions fortes et rapides de la musculature intrinsèque oculaire qui provoque de très fines et fugitives hyperophtalmotonies.

— Le rapprochement du punctum proximum est dû à l'état de spasme ou crampe accommodative, c'est-à-dire à l'état de contracture soutenue du muscle ciliaire, qui manifeste de la sorte un spasme myopigène.

— L'effacement passager de l'image vue comme à travers un brouillard fugitif,

— L'apperception visuelle fugitive,

— L'instabilité de la vision claire de près, passagère, au début et accentuée, plus tard, pour lire, dessiner et, en général, suivre tous les détails rapprochés,

— L'instabilité de la vision claire de loin, passagère, au début et accentuée, plus tard (a) soit pour suivre les images au cinématographe, à la télévision, au théâtre, en amphithéâtre, en classe, etc., avec la préférence de rester au fond de ces différentes pièces, (b) soit pour suivre le défilé rapide des maisons, des arbres, des poteaux télégraphiques, etc., vus d'un véhicule en marche, avec les sensations de « mal visuel du passager pendant le décollage et l'atterrissage », « mal visuel de train », « mal visuel d'automobile », « mal visuel de fiacre », (c) soit pour suivre le va-et-vient de la foule dans la rue, avec la sensation de « peur des espaces pleins de foule » (cirque, etc.) — sorte « d'agoraphobie visuelle » — avec la préférence des rues moins peuplées ou même désertes.

— Le vertige d'origine visuelle, passager au commencement et tenace plus tard,

— Parfois la titubation,

Tous ces symptômes sont dus à l'alternance de contraction et de relâchement du muscle ciliaire et en général à l'état d'asthénopie — état dans lequel la vue est incapable d'une application soutenue — et

en special a l etat d'asthenopie accommodative c est a dire à l asthenopie qui survient dans l hypermetropie a la suite de la fatigue causée par l accommodation autrement dit l asthenopie accommodative c est l etat d incapacite de contraction du muscle ciliaire dans les intensites correspondentes à la mise a point de l image

— La myodesopsie ou les mouches volantes representent l apparition dans le champ visuel des micro scotomes positifs mobiles, comme des points noirs isoles ou agglomerés en chaine ou en amas, il s agit des elements figures du sang qui — passant à travers les stomates des vaisseaux des proces ciliaires au cours de leurs variables tensions determinees par les mouvements accommodatifs du muscle ciliaire — sont arrives dans le corps vitre, ou, bien qu invisibles a l ophtalmoscope par leurs mouvements selon les lois combinees de l inertie et de la gravitation des corps legèrs dans les liquides, ils provoquent par leurs ombre projetee sur la retine la sensation visuelle decrite

Ce phénomene apparait donc facilement expliquable dans l hypertension retinienne provoquee ou aggravee en cas de préexistence

— La photophobie legère au commencement et tenace plus tard, est due en partie a la contraction penible et meme douloureuse des muscles irien et ciliaire fatigues déja par l accommodation

— Les crampes oculaires douloureuses

— La myalgie legere des droits internes aux mouvements des globes dans l orbite, a l occasion de *leurs sollicitations* l un apres l autre ou ensemble

— Les douleurs oculaires aux mouvements des globes dans l orbite

— Les douleurs retro oculaires

— La diplopie passagere *sans remission pendant toute la vie*, qui apparait soit au reveil *surtout* le matin comme diplopie de bonjour soit au courant de la journee en des durees variant de quelques secondes jusqu a quelques minutes et cessant generalement après un effort de fixation de l image apparue double

Tous ces *symptomes sont* dus a la sur sollicitation synchronique a l acte accommodatif de la musculature peri oculaire striee C est ainsi que la diplopie passagere et sans remission pendant toute la vie doit etre consideree specialement comme une manifestation tipique de la fatigue extreme des muscles convergents sur sollicites en opposition a *la diplopie temporaire* par deplacement du globe du à la paralysie oculo-motrice ou a une bride cicatricielle dont la fausse image s attenue ou disparait par accoutumance neutralisation ou guerison La *myalgie* accentuee des droits *interns* se manifeste surtout comme suite des efforts energiques et repétes de convergence qui tendent a situer en strabisme convergent consecutif les yeux hypermetropiques Si a l etat de contracture de la musculature peri-oculaire s ajoute aussi une

ténonite rhumatismale ou même une cellulite orbitaire, les deux discrètes, alors on s'explique pourquoi les douleurs oculaires et rétro oculaires deviennent extrêmement violentes au cours des mouvements des globes oculaires

— La nécessité d'appuyer sur les yeux avec les doigts chauffés rapidement à une source proche de chaleur bec, fourneau, calorifère, etc., est due au fait que la pression sur un muscle spasmé le décontracte et en même temps la chaleur aide au rétablissement de la circulation locale

— La sensation de fatigue palpébrale et oculaire,

— La préférence de garder fréquemment les paupières fermées pour " se reposer la vue ",

— Parfois le tic blépharo spastique,

— Parfois le faciès de névrose asthénopique, hypermétropique— instale à la longue et plus évident pendant l'acte de regarder de près — aux suivantes particularités (a) sourcils abaissés à pli vertical du tégument inter sourcilier avec des douleurs, consécutives sur sourcilières, (b) face légèrement contractée, ou même crispée, avec l'aspect concentré du visage, (c) myosis avec l'aspect sévère du regard

— Parfois les spasmes faciaux, légers, divers, accompagnant les tics blépharo spastiques,

Tous ces symptômes sont le résultat du procès physiologique normal de baisse temporaire de la capacité de travail de la musculature intra et extra oculaire ainsi que de leurs incapacité, conjointement avec celle de la face consécutivement aux activités conjuguées, particulières, prêtées par celles ci La fatigue de la musculature extra oculaire prend son origine dans les mouvements du globe oculaire poursuivant l'image Ainsi des enregistrements cinématographiques ont démontré qu'au cours de l'observation au radar, l'oeil ne suit pas continuellement le spot lumineux en mouvement sur l'écran, mais se déplace d'une manière désordonnée effectuant un nombre considérable de mouvements alternatifs dans toutes les directions (circulaire linéaire ou combiné), en secousses plus ou moins rapides, d'amplitude et fréquences variables L'attention soutenue que demande le rythme toujours rapide, dans lequel se succèdent, en un très bref laps de temps, ces stimulus répétés, provoque une instabilité progressive de fixation qui mène à l'épuisement de la fonction visuelle (1) (2)

— Les maux de tête passagers,

— La douleur frontale en barre,

— La douleur aux tempes,

(1) Berest N, Gibert A P, Perdriel G. Étude analytique des facteurs d'asthénopie oculaire chez les lecteurs de scopes radar La Médecine Aéronautique 1956 XI 2 pp 197 214

(2) Berest N, Gibert A P, Perdriel G. Prévention de la fatigue visuelle chez les lecteurs de scope radar La Médecine Aéronautique 1956 XI 4 pp 403-412

PATHOGENESIS AND AETIOLOGY OF EALES'S DISEASE

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The pathogenesis and aetiology of Eales's disease have been well summarised in several recent papers, such as those of Jefferson and Cloake, 1952, Elliot, 1954, Kimura, Carricker and Hogan, 1956, White, 1961, and especially those of Donders, 1958 and Godde Jolly, 1961, and they have much simplified the task of preparing my own account and interpretation of these complex problems

Eales's disease as originally described in 1880-2 — recurrent peripheral retinal haemorrhages in young males — cannot now be regarded as an entirely separate entity, for many cases have since been described in which the central vessels of the fundus were primarily involved (Gilbert, 1913 a,b, Siegrist, 1913, Davis, 1920, Ballantyne and Michaelson, 1937) In a particularly instructive case—a boy of 14 years old — reported by Lyle and Wybar (1961) the disease was peripheral in one eye and central in the other, which would seem to identify both types as manifestations of the same underlying condition Nor can it be said that the disease is confined to young males for numerous cases of older ages and both sexes have been described Nevertheless it remains true that the disease occurs typically in the peripheral retina and that young males are predominantly affected, and I feel it would be wiser to retain the eponymous and noncommittal name of Eales's disease, rather than adopt the later term of "retinal vasculitis" First, because retinal vasculitis is a histopathological finding which is not necessarily synonymous with the ophthalmoscopic observation of retinal sheathing, secondly, because histopathological examination of cases of Eales s disease have not always shown a vasculitis, and, thirdly, because retinal vasculitis is common in ocular pathology quite apart from Eales s disease

Retinal vasculitis, for instance, may frequently be demonstrated histologically in endophthalmitis from any cause, or in association with uveitis of such widely differing aetiology as sarcoidosis, syphilis sympathetic ophthalmitis (Eccheverria, 1922) or phacoanaphylactic reactions An attempt has been made to segregate this group as "secondary vasculitis" to differentiate it from ' primary vasculitis or Eales's disease, but we cannot yet rule out the possibility that Eales's disease may itself be secondary to uveitis, especially anterior uveitis This association has frequently been noted in the past, and

— La cephalee occipitale

— La cephalee diffuse tenace, d habitude au courant de la deuxieme moitié de la journee ou a la fin de la journee du travail visuel,

— Les etats migraineux non definis

— L état de malaise,

— L hemicranie du cote de l oeil directeur soit sur un meme fond hypermetropique bilateral soit sur un fond anisometropique,

— Parfois La migraine ophtalmique atipique fugitive mani festee par des hemianopsies homonymes partielles des scotomes scintillants atypiques et des cephalees instables en fait de moment d apparition duree et siege

— La somnolence continuelle et le besoin imperieux de dormir apres quelques heures de travail visuel

— La fatigue generale

— Le complexe d infériorite par incapacite de devisager son interlocuteur parce que cela provoque un larmoiement intense et une douleur oculaire

— Les etats asthenico depressifs

— Les etats d inquietude

— Les etats d irrascibilite

Tous ces symptomes sont dus a l excitation centrale realise a son tour par les incitations du ganglion ciliaire transmises au cortex, soit par voie directe cilio corticale soit par voies indirectes reliant au cortex les viscères sujettes aux troubles reflexes cilio visceraux ces troubles reflexes expliquent et justifient en fin de compte les quatre derniers complexes psychiques

— L inapétence

— La nausee discrete au commencement et tenace plus tard

— Les vomissements

Tous ces symptomes sont dus aux reflexes cilio digestifs

— Parfois L hypertension rétinienne provoquee ou aggravee en cas de preexistence

— Parfois Les troubles inconstants du rythme cardiaque

Ces deux symptomes sont dus aux reflexes cilio-vasculaires

En ce qui concerne specialement l hypertension retinienne il faut retenir que la nevrose du travail visuel intense et minutieux de l hyper metropie non corrigee

1 Peut devenir *la cause* d une hypertension arterielle generale, qui se manifeste au fond de l oeil comme *toute angiopathie retinienne hypertensive reversible*

2 *Aggrave* l hypertension arterielle generale *en evolution* et se manifeste au fond de l oeil sous *une forme beaucoup plus marquée* qu elle ne le ferait si la meme hypertension n était pas aggravee par la névrose hypermetropique

tenonite rhumatismale ou meme une cellulite orbitaire, les deux discretes, alors on s'explique pourquoi les douleurs oculaires et retro oculaires deviennent extremement violentes au cours des mouvements des globes oculaires

— La necessite d'appuyer sur les yeux avec les doigts chauffes rapidement a une source proche de chaleur bec, fourneau, calorifere, etc , est due au fait que la pression sur un muscle spasme le decontracte et en meme temps la chaleur aide au retablissement de la circulation locale

— La sensation de fatigue palpebrale et oculaire,

— La preference de garder frequemment les paupieres fermees pour "se reposer la vue",

— Parfois le tic blepharo spastique,

— Parfois le facies de nevrose asthenopique, hypermetropique— instable a la longue et plus evident pendant l'acte de regarder de pres — aux suivantes particularites (a) sourcils abaisses a pli vertical du tegument inter sourcilier avec des douleurs, consecutives sur sourcilieres, (b) face legerement contractee, ou meme crispee, avec l'aspect concentre du visage, (c) myosis avec l'aspect severe du regard,

— Parfois les spasmes faciaux, legers, divers, accompagnant les tics blepharo spastiques,

Tous ces symptomes sont le resultat du proces physiologique normal de baisse temporaire de la capacite de travail de la musculature intra et extra oculaire, ainsi que de leurs incapacite, conjointement avec celle de la face consecutivement aux activites conjuguees particulieres, pretees par celles ci La fatigue de la musculature extra oculaire prend son origine dans les mouvements du globe oculaire poursuivant l'image Ainsi des enregistrements cinematographiques ont demontre qu'au cours de l observation au radar, l'oeil ne suit pas continuellement le spot lumineux en mouvement sur l'ecran, mais se deplace d'une maniere desordonnee, effectuant un nombre considerable de mouvements alternatifs dans toutes les directions (circulaire, lineaire ou combinee), en secousses plus ou moins rapides d'amplitude et frequences variables L'attention soutenue que demande le rythme toujours rapide dans lequel se succedent, en un tres bref laps de temps, ces stimulus repetes, provoque une instabilite progressive de fixation, qui mene a l epuisement de la fonction visuelle [1] [2]

— Les maux de tete passagers,

— La douleur frontale en barre

— La douleur aux tempes,

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[1] Berest N Gibert A P Perdriel C Étude analytique des facteurs d asthénopie oculaire chez les lecteurs de scopes radar La Médecine Aeronautique 1956 XI 2 pp 197–214

[2] Berest N Gibert A P Perdriel G Prevention de la fatigue visuelle chez les lecteurs de scope radar La Médecine Aéronautique 1956 XI 4 pp 403-412

attirent en même temps l'attention que la durée d'adaptation visuelle est de beaucoup supérieure à celle de l'adaptation auditive. Ils démontrent que le bruit des moteurs doit toujours être compris entre 85 et 95 db globaux, c'est-à-dire au dessous des valeurs qui provoquent l'inadaptation de la vue. Mais Svetlakov et Bolsakov (1) dans leur étude de 1957, *démontrent que la diminution de l'ouïe aux travailleurs des stations de radiolocation* est le résultat de la fatigue de l'analysateur auditif à cause de l'action du bruit monotone non interrompu, qui dépasse la valeur du seuil moyen de l'action préjudiciable du bruit qui est de 75 db, de sorte que après une journée de travail la majorité présentaient l'acuité auditive *diminuée chez toutes les fréquences* de 5 à 25 db.

Toujours dans le cadre de la vue *hypermétropique* c'est aussi intéressant à connaître l'état fonctionnel de la rétine vis-à-vis du *régime* de la lumière de la chambre obscure du radar. Zubov (2) en 1958 est arrivé à la conclusion que sous l'influence de la fatigue visuelle les seuils de la sensibilité de contraste augmentent d'habitude.

Mais d'autre part il ne faut pas oublier que dans la chambre obscure du radar il existe une très petite différence d'illumination entre le radar (1-2 lux), l'appareil azimutal (3 lux) et le *goniomètre* (6 lux), donc de l'ordre de quelques lux.

Les conditions visuelles de travail au radar sont donc tout à fait spéciales si l'on pense que pour le travail de finesse visuelle qu'il convient en typographie, *horlogerie*, gravure, couture au fil blanc sur le blanc, etc., il s'imposent 100 à 250 lux.

On sait que *l'accommodation à une faible lumière est normale, mais la désaccommodation est difficile*.

Cette situation doit être liée à la constatation qu'au début du crépuscule — lorsque diminue la capacité du sens lumineux — l'accommodation manifeste la tendance vers la réfraction de type myopique nocturne.

Donc le régime de lumière identique de la chambre obscure du radar maintient constante l'adaptation de l'oeil pendant le travail et lui évite en quelque sorte, de ce point de vue, la fatigue.

* * *

Afin de mieux comprendre en détail le symptôme suivant qui indique une très étroite liaison entre l'excitation lumineuse et les gonades, les suivantes constatations s'imposent dans le cadre de l'observation sur les écrans radar.

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(1) Svetlakov M. I., Bolsakov A. M. Sur la sensibilité auditive aux travailleurs des stations de radio-location. Voenno Med. tinskii Journal 1957, 9, pp. 31-34.

(2) Zubov V. F. Évaluation de la fatigue visuelle. Voenno Meditinskii Journal 1958, 10, pp. 53-55.

— Parfois l'exophtalmie mono latérale à peine esquissée et très passagère, est due aux réflexes cilio corticaux à effet hypertonique sur la musculature oculaire extrinsèque striée, hypertonie qui persiste seulement tant que des impulsions excitatrices agissent sur la région cortico oculomotrice du côté de l'exophtalmie. L'hypertonie passagère de la musculature oculaire extrinsèque striée explique d'ailleurs — même en l'absence de l'exophtalmie — la sensation de tension intra orbitaire passagère.

— L'adaptation diurne retardée de 10-15-30 minutes, après la sortie de la chambre obscure du radar,

— La photophobie à la lumière du jour et de la chambre,

— L'adaptation nocturne déficitaire, par perception confuse continuelle à la lumière de nuit,

Tous ces symptômes sont dus à l'insuffisance gradée de régénération de l'erythropsine, au cours de l'acte visuel hypermétropique. Ainsi l'hespéranopie ou la cécité crépusculaire ou l'amblyopie crépusculaire ou l'hypoadaptation rétinienne ou l'héméralopie ou la nyctalopie ou la cécité nocturne est la diminution considérable de la vue installée en même temps que la diminution de la lumière (crépuscule), consécutivement aux troubles fonctionnels invisibles à l'ophtalmoscope.

— Les troubles discrets dans la disposition du pigment rétinien des régions maculaire et péri maculaire, sont dus aux troubles anatomiques, visibles à l'ophtalmoscope, dans le cadre de l'hespéranopie.

Il faut souligner le fait que les facteurs généraux admis pour l'hespéranopie majeure sont la chorio rétinite, la rétinite, l'hypovitaminose A, et pour l'hespéranopie mineure ce sont les amétropies et le traumatisme lumineux répété.

Mais nous attirons l'attention, que l'adaptation à l'obscurité peut encore être empêchée aussi par l'inhibition que provoque l'excitant acoustique sur liminaire.

Dans ce sens Visnevski en 1936, Bogoslavski en 1936 et 1939, Kravkov en 1945 et Semenovskaia en 1946 [cités par Sneakin et Anisimova (2)] ont constaté que les excitations acoustiques diminuent la sensibilité à la lumière. À leur tour, Grognot et Perdriel (1) ont constaté en 1959, que le bruit expérimental, choisi de la gamme sonore de l'ambiance d'atelier, diminue fortement la capacité visuelle nocturne, ce fait influence en général les travailleurs de nuit, qui doivent conduire des voitures bruyantes et qui risquent de provoquer des accidents de transport et de circulation et influence spécialement les travailleurs des équipes de nuit qui travaillent dans les zones d'ombre dans lesquelles la discrimination de formes est très difficile. Les auteurs

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(1) Grognot P. Perdriel G. Influence du bruit sur certaines fonctions visuelles. La Méd. Aéron. 1959, 14, 1, pp. 25–30.

(2) Sneakin P. G. Anisimova A. P. Action des excitations indirectes (secondaires) sur la sensibilité à la lumière. Fiziologhiceskii Journal URSS 19 4, 41 5, p. 625.

faible et moyenne hypermetropie du radariste, prend souventes fois un aspect dramatique

En general tous les radaristes sujets aux troubles de l asthenopie accommodative et parmi ceux ci specialement les hypermetropes exasperes par l impossibilite de clairement voir les images au cours de *leur vie journaliere* accusent la lumiere en general et surtout la lumiere artificielle comme cause de leurs troubles visuels

Les brefs et frequents repos accommodatifs que ces ametropes asthenopiques s imposent suppriment rapidement les troubles de la vue qui cependant reapparaissent aussitot que le travail visuel journalier est repris

Mais pas *seulement* la *non* correction de ces vices de refraction engendre la nevrose asthenopique

Aussi l hypocorrection hypermetropique peut amener de graves desordres de nevrose asthenopique

À son tour l hypercorrection hypermetropique l hypercorrection miopique qui transforme l oeil en hypermetrope, ou l inexacte correction de l astigmatisme *peuvent provoquer ou* — en cas de preexistence — aggraver la nevrose asthenopique

Connaissant le polymorphisme symptomatique de l asthenopie accommodative en general et specialement provoque par l hypermetropie on a la possibilite d infirmer de nombreux faux diagnostics — tels que glaucome tumeur cerebrale, meningite sinusite crises d hyperthyroidisme diverses psychopaties — ainsi qu en meme temps de decouvrir le substratum materiel et de la paresse visuelle et des troubles generaux qui s y rattachent

Ainsi par exemple l hemicranie du cote de l oeil directeur soit sur un meme fond hypermetropique bilateral soit sur un fond anisometropique doit toujours etre suspectee comme d origine *asthenopique* avant meme de penser a un glaucome

Mais il faut aussi tenir compte du fait que *la nevrose asthenopique peut soit aggraver des maladies preexistentes oculaires ou generales dont l acuite des symptômes n a pu etre rapportee jusqu à present à leur vraie cause soit favoriser l apparition de ces maladies ou justifier le mecanisme inconnu de certaines autres maladies*

Pour ce qui est de l aggravation des maladies oculaires ou de leur favorisation toute infection conjonctivale et palpebrale — pour prendre le plus simple exemple — rebelle a la therapeutique habituelle ou apparue intempestivement doit nous suggerer un fond biologique oculaire au dessous de la normale qui permet au microbes habituels de s exacerber la virulence ce qui est evidemment du d abord a la fatigue de l appareil visuel en entier qu engendre l asthenopie accommodative et ensuite a la fatigue generale qui decoule des troubles a point de depart du ganglion ciliaire

Pour ce qui est de certaines maladies digestives a savoir colites gastrites ulceres gastriques et duodenaux celles ci ont beneficie de *la correction dioptrique respective* qui *a pu soit ameliorer soit même reduire*

Le fait que la lumiere influence la fonction gonadotrope de l'hypophyse a ete demontre en 1937 par J Benoit et l'influence de la lumiere et de la temperature, dans le determinisme des modifications saisonnieres de la secretion d'hormone gonadotrope hypophysaire a ete mise en evidence en 1939 par Kabak et Tereza (1)

D'autres recherches, etudiant les suites de l excitation du nerf optique sur l'hormonogenese adeno hypophysaire, ont demontre que l excitation du nerf optique, avec un courant d induction, ou l'illumination de l'oeil avec une lumiere monochromatique, modifie d'une maniere reflexe la fonction melanophore et gonadotrope de l'hypophyse (2), tandis que l'hypophysectomie pratiquee a la *rana temporana* adulte provoque l'inhibition du cycle sexuel, l'involution des glandes genitales et la regression totale des caracteres sexuels secondaires [Gallien cite par Vivien et Schott (3)]

L'application pratique des actions stimulatrices de la lumiere est actuellement largement utilisee en zootechnie pour l'augmentation de la production des oeufs aux volailles (4) (5), pour l augmentation de la fecondite et de la production de lait aux vaches (6), dans le meme ordre d'idees, il apparait comme tres interessante l observation que de tous les cochonnets mis dans de differentes conditions de lumiere, le groupe de ceux maintenus dans des boxes lumineuses manifeste une importante augmentation de leur poids hypophysaire et testiculaire (5)

Les faits ci dessus exposes nous montrent l influence que peut avoir la presence de l excitation lumineuse sur les gonades par l intermede de l'hypophyse

C est ainsi que nous pouvons nous expliquer le symptome rencontre chez quelquesuns des operateurs de radar a savoir la diminution de la capacite sexuelle

En verite, celle ci parait justifiee par l absence de l excitation lumineuse normale sur la fonction gonadotrope de l hypophyse, au cours du sejour prolonge et pendant longtemps, dans la chambre obscure du radar

Diversite clinique de la nevrose asthenopique

L asthenopie accommodative de tout astigmate mixte, de tout astigmate hypermetropique simple et compose, ainsi que surtout de la

(1) Kabak I M Tereza S I Travaux sur la dynamique du developpement Medghiz 1939 II

(2) Sudakova A D Les theses du rapport de la session scientifique L hypophyse (Physiologie pathologie clinique) 18-21 XII 1957 Medghiz

(3) Vivien J H Schott J Contribution à l etude des corrélations hypothalamo pituitaires chez les batraciens Le controle de l activite gonadotrope Journ de Physiologie 1958 L 2 pp 561-563

(4) Borison V A Jivotnovodstvo 1958 4 p 80

(5) Karapetian S K D A N URSS 1954 3 p 585

(6) Sveein K B Refer J Biol 1957 18 p 435

2 Admission des hypermetropes corriges jusqu'a + 1 5 d sph, dans les suivantes conditions

(a) La distance d entre l oeil et l ecran radar doit etre de 30 jusqu a 40 cm et pour empecher une plus grande proximite de l ecran (2) *donc pour eviter la sur accommodation inutile*, il s impose un limitateur de tete (4)

(b) Les punctums proximus (1) de l accommodation ne doivent pas depasser 13 cm a 20 ans, 16 cm a 30 ans et 24 cm a 40 ans et de la convergence ne doit pas depasser 11 cm

(c) La duree du travail accommodatif sera de 1 1/2 jusqu a 2 heures

(d) L amelioration des deficiences conjonctivales et corneennes *par alimentation* abondante en vitamine B_2 qui entretient la vitalite de la conjonctive et de la cornee la carence de cette vitamine aggravant les troubles conjonctivaux decrits consecutivement a la stase des vaisseaux locaux et realisant ici un punctus minoris resistentiae favorable aux degenerations combinees aux infections (2)

(e) L amelioration de la fatigue accommodative par alimentation riche en vitamines B_1 et C la vitamine B_1 — selon Sysy (3) augmente rapidement l amplitude de l accommodation apres 30 minutes depuis l injection et dure jusqu a 4–5 jours la dose journaliere normale necessaire pour l homme actif etant de 2 mg la vitamine C possede l action de *maintenir augmentée* l amplitude de l accommodation, la dose journaliere normale necessaire pour l adulte etant de 30 a 75 mg

N B Les affections qui impliquent l elimination ou la non resorbtion de ces vitamines sont contre indiquees dans la selection des *radaristes* (2)

(f) Le repos accommodatif pour le reste de la journee par le port obligatoire permanent des lunettes respectives de correction pour le pres par le regard a grande distance — qui relache le muscle ciliaire — des paysages lointains et par le sommeil (2)

II Dans *le cadre therapeutique general* de la nevrose asthenopique, les mesures a prendre sont les suivantes

A Mesures a application strictement oculaire

1 *Lentilles correctes* Au commencement il se peut que la correction optique aggrave meme un peu les reflexes cilio visceraux parce que le muscle ciliaire se contracte a peu pres toujours avec la meme intensite qu avant et les verres augmentent donc *passagerement* l ametropie, d ou exageration de ces reflexes

Une a deux semaines constituent en general la periode necessaire pour s habituer aux lunettes apres quoi les malades bien portants prennent parfois meme du poids

D autre part il faut savoir que les lunettes prescrises pendant toute maladie en general et asthenisante specialement — lorsque le tonus du muscle ciliaire etait diminue — sont plus fortes que celles

le temps de la guérison de ces maladies, ou les deux ensemble, ce qui démontre que *la présence des réflexes cilio digestifs empire ces maladies, soit en les aggravant, soit en leur prolongeant le temps de la guérison, ou les deux ensemble*

Il reste à étudier si, en fin de compte, ces réflexes cilio digestifs ne seraient pas capables de provoquer même *per primam* la lésion organique des maladies digestives ci dessus citées!

Les réflexes cilio corticaux, qui naissent en même temps, aggravent ces symptômes et compliquent parfois ces maladies par des phénomènes de névrose asthénique sans ou avec manifestations psychopathiques

Mais jusqu'ici on a seulement tenu compte de ce que peut provoquer la névrose asthénopique

Il devient donc nécessaire de signaler aussi *l'apparition de cette névrose sous l'influence des affections asthénisantes*, à savoir l'hépatite épidémique, la grippe, les maladies infectieuses chroniques, l'avitaminose, les opérations, la convalescence traînante après infections graves et tout autre motif qui détermine la baisse de l'état général

Thérapeutique des troubles visuels et généraux associés engendrés par le radar

I *La correction dioptrique*, qui s'impose en premier lieu, donne des résultats impressionnants de récupération de la santé générale et de la capacité de travail visuel en particulier

En adoptant les idées de Berest, Curveille, Perdriel (1), Visnevski, Petrenko (4), Sysi (cité par 3), et ajoutant d'autres, avec mes collaborateurs Popesco, Stefan, Bengulesco, Musetesco, nous avons établi les suivantes mesures thérapeutiques (2)

I Vérification minutieuse de l'acuité visuelle, après quoi on décide a L'élimination (1) des hypermétropes au dessus de + 1,5 d sph, des astigmates hypermétropiques simples et composés, des astigmates myopiques simples au dessus de — 1 d sph et composés, des astigmates mixtes, b L'admission (1) des emmétropes, des hypermétropes jusqu'à + 1,5 d sph, mais toujours corrigés, des astigmates miopiques simples conformes à la règle et inférieurs à — 1 d, des myopes de — 1 d sph — 2 d sph, — 3 d sph sans choroïdose, qui sont les plus indiqués de ceux à l'acuité visuelle pour chaque oeil de 1/2 sans correction jusqu'à 9/10 avec correction

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(1) Berest N Curveille J Perdriel G Les normes d'aptitude visuelle des lecteurs de scope radar La Médecine Aéronautique 1958 XIII 3 pp 265 270

(2) Carapancea M Popesco M Stefan M Bengulesco D Musetesco St Les troubles visuels et leurs conséquences sur l'organisme dans les conditions de perception au dispositif radar Communication présentée à l'*Institut de Physiologie Normale et Pathologique D Danielopolu de l'Académie de la République Populaire Roumaine*, dans la séance du 1 VI 1961 sous la présidence du Directeur de l'Institut l'Académicien Prof Dr Gr Benetato

(3) Mutze K Die Akkommodation des menschlichen Auges Berlin Akademie—Verlag 1956 pp 137

(4) Visnevski N A Petrenko G S Observations ophtalmologiques sur les travailleurs des stations de radiolocation Voenno Meditinskii Journal 1958 10 pp 53–55

2 Admission des hypermetropes corriges jusqu a + 1 5 d sph dans les suivantes conditions

(a) La distance d entre l oeil et l ecran radar doit etre de 30 jusqu a 40 cm et pour empecher une plus grande proximite de l ecran (2) donc pour eviter la sur accommodation inutile il s impose un limitateur de tete (4)

(b) Les punctums proximus (1) de l accommodation ne doivent pas depasser 13 cm a 20 ans 16 cm a 30 ans et 24 cm a 40 ans et de la convergence ne doit pas depasser 11 cm

(c) La duree du travail accommodatif sera de 1 1/2 jusqu a 2 heures

(d) L amelioration des deficiences conjonctivales et corneennes par alimentation abondante en vitamine B_2 qui entretient la vitalite de la conjonctive et de la cornee la carence de cette vitamine aggravant les troubles conjonctivaux decrits consecutivement a la stase des vaisseaux locaux et realisant un *punctus minoris resistentiae* favorable aux degenerations combinees aux infections (2)

(e) L amelioration de la fatigue accommodative par alimentation riche en vitamines B_1 et C la vitamine B_1 — selon Sysy (3) augmente rapidement l amplitude de l accommodation apres 30 minutes depuis l injection et dure jusqu a 4–5 jours la dose journaliere normale necessaire pour l homme actif etant de 2 mg la vitamine C possede l action de maintenir augmentee l amplitude de l accommodation, la dose journaliere normale necessaire pour l adulte etant de 30 a 75 mg

N B Les affections qui impliquent l elimination ou la non resorbtion de ces vitamines sont contre indiquees dans la selection des radaristes (2)

(f) Le repos accommodatif pour le reste de la journee par le port obligatoire permanent des lunettes respectives de correction pour le pres par le regard a grande distance — qui relache le muscle ciliaire — des paysages lointains et par le sommeil (2)

II Dans *le cadre therapeutique general* de la nevrose asthenopique, les mesures a prendre sont les suivantes

A MESURES A APPLICATION STRICTEMENT OCULAIRE

1 *Lentilles correctes* Au commencement il se peut que la correction optique aggrave meme un peu les reflexes cilio visceraux, parce que le muscle ciliaire se contracte a peu pres toujours avec la meme intensite qu avant et les verres augmentent donc *passagerement* l ametropie d ou exageration de ces reflexes

Une à deux semaines constituent en general la periode necessaire pour s habituer aux lunettes apres quoi les malades bien portants prennent parfois meme du poids

D autre part il faut savoir que les lunettes prescrises pendant *toute* maladie en general et asthenisante specialement — lorsque le tonus du muscle ciliaire etait diminue — sont plus fortes que celles

le temps de la guérison de ces maladies, ou les deux ensemble, ce qui démontre que *la présence des réflexes cilio digestifs empire ces maladies, soit en les aggravant, soit en leur prolongeant le temps de la guérison, ou les deux ensemble*

Il reste à étudier si, en fin de compte, ces réflexes cilio digestifs ne seraient pas capables de provoquer même *per primam* la lésion organique des maladies digestives ci dessus citées !

Les réflexes cilio corticaux, qui naissent en même temps, aggravent ces symptômes et compliquent parfois ces maladies par des phénomènes de névrose asthénique sans ou avec manifestations psychopathiques

Mais jusqu'ici on a seulement tenu compte de ce que peut provoquer la névrose asthénopique

Il devient donc nécessaire de signaler aussi *l'apparition de cette névrose sous l'influence des affections asthénisantes*, à savoir l'hépatite épidémique, la grippe, les maladies infectieuses chroniques, l'avitaminose, les opérations, la convalescence traînante après infections graves et tout autre motif qui détermine la baisse de l'état général

Thérapeutique des troubles visuels et généraux associés engendrés par le radar

I *La correction dioptrique*, qui s'impose en premier lieu, donne des résultats impressionnants de récupération de la santé générale et de la capacité de travail visuel en particulier

En adoptant les idées de Berest, Curveille, Perdriel (1), Visnevski, Petrenko (4), Sysi (cité par 3), et ajoutant d'autres, avec mes collaborateurs Popesco Stefan, Bengulesco, Musetesco, nous avons établi les suivantes mesures thérapeutiques (2)

1 Vérification minutieuses de l'acuité visuelle, après quoi on décide a L'élimination (1) des hypermétropes au dessus de + 1,5 d sph, des astigmates hypermétropiques simples et composés, des astigmates myopiques simples au dessus de — 1 d sph et composés, des astigmates mixtes, b L'admission (1) des emmétropes, des hypermétropes jusqu'à + 1,5 d sph, mais toujours corrigés, des astigmates miopiques simples, conformes à la règle et inférieurs à — 1 d, des myopes de — 1 d sph — 2 d sph, — 3 d sph, sans choroïdose, qui sont les plus indiqués, de ceux à l'acuité visuelle pour chaque oeil de 1/2 sans correction jusqu'à 9/10 avec correction

(1) Berest N Curveille J Perdriel G Les normes d'aptitude visuelle des lecteurs de scope radar La Médecine Aéronautique 1958 XIII 3 pp 265-270

(2) Carapancea M Popesco M Stefan M Bengulesco D Musetesco St Les troubles visuels et leurs conséquences sur l'organisme dans les conditions de perception au dispositif radar Communication présentée à l'*Institut de Physiologie Normale et Pathologique D Danielopolu de l'Académie de la République Populaire Roumaine* dans la séance du 1 VI 1961 sous la présidence du Directeur de l'Institut l'Académicien Prof Dr Gr Benetato

(3) Mutze K Die Akkommodation des menschlichen Auges Berlin Akademie-Verlag 1956, pp 137

(4) Visnevski N A Petrenko G S Observations ophtalmologiques sur les travailleurs des stations de radiolocation Voenno Meditinskii Journal 1958 10 pp 53-55

stressed again recently by Davenport (1954) who pointed out that both retina and uvea may be inflamed together or alternately, and by Godde Jolly (1961) who observed uveitis in 30 per cent of his cases In fact the significance of this relationship may be missed since long intervals may separate the two inflammations A further difficulty is that retinal vasculitis of the kind seen in multiple sclerosis which is not secondary to uveitis, and would therefore have to be classified as primary ', is certainly not in the same clinical category as Eales's disease

PATHOLOGY

In considering the pathogenesis of Eales's disease we are much handicapped by the difficulty in obtaining pathological material at a sufficiently early stage to determine the natural history of the disease or even to decide with certainty whether it may have a single cause or multiple causes Most of the globes which have been examined histologically had been removed in the final stages of retinal detachment or of glaucoma when the initial process may well have long subsided Donders (1958) has already thoroughly analysed the 107 histo pathological reports in the literature, about one third of these fall into the classical picture of Eales's disease and two thirds were cases of retinal vasculitis undoubtedly secondary to uveitis

These reports have shown the pathology of Eales's disease to be variable but briefly the predominant feature has been a patchy perivascular or intramural infiltration of lymphocytes (Fig 1) or of granulation tissue occasionally with but usually without, giant cells (Fig 2) Eosinophils have not been remarked upon, and were presumably not a feature of the reaction — a point of distinction from peri arteritis nodosa Plasma cells on the other hand, are not uncommon



FIG 1 Retinal periphlebitis in endophthalmitis phacoanaphylactica. Note the marked lymphocytic infiltration around the vein while the artery is little affected Haematoxylin and eosin. x 75

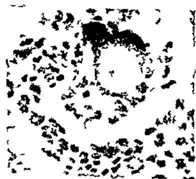


FIG 2 Granulomatous reaction in a case of Eales's disease This focus of lymphocytes endothelioid cells and a giant cell was found near a vein. P.A.S and Haematoxylin x 4 0

considerent qu aux nevrotiques il existerait un desequilibre entre le cortex et les regions sous — corticales avec la mise en liberte des dernières vis a vis du controle cortical celles ci en etat d excitation augmentee, travaillent anarchiquement les ordres transmises a la periphérie dans ces conditions sont depourvus de l action corrective discriminatrice de l ecorce cerebrale

Mais ces troubles generaux et les trobles oculaires — dont specialement le muscle ciliaire fatigue et epuise par ses rapides contractions continuellement repetees — beneficieront de la correction dioptrique qui est leur traitement specifique

Le but de cette correction dioptrique dans l hypermetropie est de suppler l amplitude de l accommodation pour faire face au nouveau pourcentage d hypermetropie latente devenue hypermetropie manifeste La correction de la nouvelle hypermetropie manifeste empeche la contraction du muscle ciliaire au dela de ses limites physiologiques et donc aussi la fatigue qui s ensuit dans tous les elements oculaires ce qui en fin de compte n excite plus anormalement le ganglion ciliaire pour declencher ses reflexes

En meme temps la correction dioptrique empeche l incapacite du muscle ciliaire de mettre continuellement a point l image sur la retine et par consequent empeche l alternance des images brouillees et claires qui provoquent aussi de cette maniere un autre etat de nevrose, mais cette fois ci purement visuel

2 *Evitement de tout autre facteur nevrotique*

III *Les phenomenes d incapacite adaptative retinienne* seront empeches par les suivantes mesures therapeutiques

1 Preadaptation graduelle à l obscurite avec la protection du regard envers la lumiere intense du jour par

(a) l emploi obligatoire 20 minutes avant d entrer dans la chambre obscure du radar de visiere protectrice à philtre de lumiere et de lunettes fumees à 75% absorbtion ensuite

(b) L emploi obligatoire 30 minutes avant d entrer dans la *chambre obscure du radar — selon Platonov* [1] — de lunettes rouges rubis ou l accommodation préalable dans la chambre a la lumiere rouge

2 Desadaptation graduelle a l obscurite — consistant de la prevenance de la sensation d eblouissement lumineux associee aux contractions — decontractions brusques du muscle ciliaire fatigue par l effort accommodatif déployé dans la chambre obscure — par le port obligatoire de la visiere et des lunettes a philtres de lumiere apres etre sorti de la chambre obscure pendant 10–15–30 minutes, le myope gardera continuellement bien entendu comme d habitude a la

[1] Platonov K L homme en vol Bucarest Ed Mil du Min des Forces Armées de la R P R 1959

dont a besoin le même malade plus tard après sa guérison, lorsque le muscle ciliaire retrouve son tonus normal. C'est pour cela que les lunettes prescrites pendant la maladie sont plus fortes de + 0,50 d. sph. jusqu'à + 2,5 d. sph., vis-à-vis des lunettes nécessaires au même organisme rétabli.

Cela explique aussi pourquoi en plein état de santé les jours où on est fatigué, les même lunettes ne sont pas aussi bonnes qu'aux jours où l'on n'est pas fatigué.

2. *Verres protecteurs* pour atténuer l'éclat de la lumière du soleil et de la neige, mais seulement dans les conditions indiquées plus bas (III).

3. *Position habituelle de l'observateur pendant la lecture*. Observateur en faible illumination, tandis que la lumière, qui baigne le livre regardé, vient de derrière et de la gauche de l'observateur, ou de n'importe où, par l'entremise d'un abat-jour, le livre se trouvant compris dans une plage de lumière, tandis que l'observateur reste en pleine obscurité.

4. *Douche progressivement échauffée jusqu'à la limite supportable, pendant tout au plus une minute, ensuite refroidissement graduel jusqu'à la température normale, sur les yeux fermés et la face*. Ces lavages seront faits le soir, une heure au moins avant le coucher, pour que la circulation des liquides intra-oculaires ne stagne pas avec le sommeil, mais continue de la sorte encore pendant quelques temps la décongestion de l'oeil en général et de la musculature intra-oculaire, en spécial.

5. *Sommeil* — de préférence — naturel et suffisamment long, le relâchement le plus physiologique du muscle ciliaire, car le muscle ciliaire en général et spécialement le muscle ciliaire de l'hypermétrope ne se repose que pendant le sommeil » (1).

B. MESURES À APPLICATION STRICTEMENT GÉNÉRALE

1. *Administration des tranquilisants centraux et périphériques conjointement à la correction dioptrique*. La névrose asthénopique est une maladie oculaire par sur-sollicitation visuelle à troubles ultérieurs organiques généraux, dont le reflet cortical trouble de plus encore la fonction visuelle, qui aggrave les troubles généraux, qui aggravent de nouveau les troubles oculaires, donc un véritable cercle vicieux qui peut être interrompu en soignant en même temps et les troubles généraux et spécialement les troubles oculaires.

Les troubles généraux, qui ne sont autre chose que des réflexes cilio-viscéraux et cilio-cortico-viscéraux à reflet viscéro-ciliaire et viscéro-cortico-ciliaire, seront soignés par des tranquilisants centraux et périphériques.

D'ailleurs Bikov et Kurtin (2) qui se sont occupés des relations cortico-viscérales dans des conditions normale et pathologiques

(1) Guillaumat L., Schiff-Wertheimer S., Offret G., Dubois-Poulsen A. Ophtalmologie. Ed. Méd. Flammarion 1953, p. 58.

(2) Bikov K. M., Kurtin S. I. La théorie cortico-viscérale de la pathogénie de la maladie ulcéreuse. Bucarest. Ed. de l'Etat 1954.

Il s agit surtout de l incapacite du muscle ciliaire a faire face a la transformation d un certain pourcentage d hypermetropie latente en hypermetropie manifeste

L oscilation tonique irreguliere du muscle ciliaire fatigue, qui, spontanement et en de tres variables durees se relache et puis reprend plus ou moins completement son tonus normal realise une alternance irregulierement brouillee et claire des images Mais *justement cette defection informative des centres visuels est un autre mecanisme pathogenique de l etat de nevrose cette fois ci purement visuel qui explique tres bien aussi de cette maniere ci les desordres vegetativo psychiques*

La conclusion generale sur la therapeutique curative des troubles de la névrose asthenopique, est qu on doit guerir la fatigue du muscle ciliaire d abord et ensuite les troubles generaux associes non gueris par la correction dioptrique et les autres mesures therapeutiques oculaires

Aujourd hui les recherches de physiologie oculaire experimentales et cliniques devoilant le mecanismes des desordres ametropiques a participation si diverse et si importante de tout l organisme imposent de diagnostiquer ces phenomenes

Donc pour depister les vices de refraction qui peuvent se manifester parfois par de si graves troubles de nevrose asthenopique et afin d instituer une therapeutique preventive une minutieuse verification de l etat visuel devient obligatoire pour le radariste Cela d autant plus que ces vices de refraction muets d habitude sont decouverts soit tout a fait accidentellement soit a l occasion des troubles visuels survenant après des efforts visuels prolonges ou à la suite d affections generales asthenisantes

* * *

À la fin de ce travail il faut ajouter que ces recherches ont pu etre effectuées grace a l appui de l Academicien Gr Benetato et grace a l aide du Lt Colonel Al Ionasco Chef du Service Medical de l Aviation

Pour l aide apporte au present travail nous remercions chaleureusement l ingenieur D Bengulesco et le docteur St Musetesco

Travail du Laboratoire de Physiologie et Physiopathologie Oculaire Clinique et Experimentale de l Institut de Physiologie Normale et Pathologique Daniel Danielopolu de l Academie de la Republique Populaire Roumaine

Directeur de l Institut Academicien Prof Dr Gr Benetato

lumière du jour, les lunettes de correction respective, légèrement fumées, pour la vue de loin

3 Amélioration de l'adaptation par l'alimentation riche en vitamine A, en même temps c'est évident qu'on n'admettra jamais les blonds à peau blanche, à iris de couleur claire et à fond d'oeil discrètement pigmenté, donc ceux qui par leur constitution se trouvent dès le commencement au dessous du niveau biologique exigé à un individu à réactions d'adaptation normale vis à vis de la lumière et de l'obscurité

IV *La diminution de la capacité sexuelle déterminée par l'obscurité prolongée* sera empêchée par les suivantes mesures thérapeutiques

1 La durée du travail dans la chambre obscure ne dépassera pas journellement 1 1/2 jusqu'à 2 heures

2 Le port de la visière protectrice à philtre de lumière et des lunettes fumées doit se réduire chez l'hypermétrope et l'emmétrope *seulement* à 10-15-30 minutes après l'achèvement du service, afin de réaliser une désadaptation graduelle à l'obscurité et une réadaptation graduelle à la lumière, et *pas du tout au reste de la journée*

3 L'exposition de l'organisme en général et de la vue en spécial à de vraies ' bains de soleil '

V *La protection de l'organisme vis à vis des ondes ultra courtes du radar* sera empêchée d'une part par l'élimination des personnes à inclusions de fragments métalliques dans leur corps comme des prothèses, des projectiles, etc , et d'une autre part, bien entendu, de tous les objets métalliques, qui se trouveraient dans les poches dans le visières, dans les montures des lunettes, etc , toutes ces inclusions métalliques aggravant l'action des ondes ultra courtes émises par le radar [1]

VI *Les conditions du micro climat de la chambre obscure du radar* seront assurées par sa continuelle ventilation, à maintien constant, tant de la température fraîche que de l'humidité normale

Conclusions sur la physiologie oculaire clinique et la thérapeutique curative et préventive de la névrose asthénopique engendrée par le radar

La conclusion générale sur la pathogénie des troubles de la névrose asthénopique, est que la fatigue du muscle ciliaire d'abord et ensuite des autres éléments oculaires qui contribuent à la perfection de l'acte visuel, incapables d'accomplir leurs fonctions, tous ces mécanismes engendrent graduellement en fin de compte d'une part, des troubles locaux oculaires et d'autre part, par l'excitation anormale du ganglion ciliaire, des troubles végétatifs dans les organes subordonnés à l'innervation ciliaire, ainsi que des troubles de l'activité corticale, qui augmentent de plus encore les troubles végétatifs

[1] Boiteau H Les effets biologiques des ondes radar Rev des Corps de Santé des Armées 1960 I 5 pp 637-652

graduated superposed parallelly to the pupillar plane, and as near as possible to the eye — since the eye of the rabbit is oval having a vertical great axis — for commodity sake we have always measured its diameter horizontally

2° Myosis in conditions of high altitude hypobarism

In general the rabbit was left free in the barochamber, in order to observe its general behavior and at the same time, and within possibilities, the pupillar one However, the animal was sometimes immobilized without fastening its head, so as to follow bilaterally the pupillary modifications Other times the rabbit was immobilized with the head secured in flexion to the right or left, resting on the transparent window of the barochamber, for measuring precisely the modifications of the pupillary diameter

The rabbits with medicinal monolateral myosis have been subjected to very high ascents between 8 000 and 12 000 *m* corresponding to atmospheric pressures between 267 and 145 mm Hg The ascent to 8 000 m, has taken 1 min 50 sec, and the return 40 sec the ascent to 9 000 m 2 min 5 sec and the return 40 sec, the ascent to 10 000 m 2 min 24 sec and the return 44 sec the ascent to 11 000 m 2 min 40 sec and the *return* 48 sec and the ascent to 12 000 m has taken 2 min 28 sec and the return to the ground 53 sec

The most used experimental prototype has been the ascent to 9 000 m i e to 230 mm Hg atmospheric pressure, with a 3 min exposure at that altitude followed by the *return* to the ground, and a 3 min rest at normal atmospheric pressure

A total of 52 ascents were carried out with 12 animals in a state of myosis Sometimes the same animal in a state of myosis was subjected at the same sitting to 5 to 9 ascents while in an interval of 4 to 8 days, in another 3 sittings, to a total of 11 ascents

The pupillary diameter was measured in a constantly luminous condition with a metallic blade millimetrically graduated pressed against the window of the barochamber and superposed parallelly upon the horizontal pupillar plane The pupillar modifications determined by the action of high altitude hypobarism upon the rabbit in conditions of medicinal myosis have also been studied in connection with the photo motor reflex myosis caused by the 5 V focalized light of the Zeiss ophthalmoscope

THE RESULT OF RESEARCHES

1 Myosis in conditions of normal atmospheric pressure

1st Experiment One drop of 1% eserine is instilled The pupil decreases gradually from its normal horizontal slightly inconstant and around 5 mm variable diameter, to a constant horizontal diameter of

THE MECHANISM OF THE MODIFICATIONS OF PUPILLAR DIAMETER INFLUENCED BY MYOTICS ON THE ORGANISM SUBJECTED TO HIGH ALTITUDE HYPOBARISM

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(*Roumania*)

Recent experimental researches, carried out in our Institute, have shown that the eye, in general, and particularly the dynamic modifications of the iris musculature constitute a precise and delicate indicator of modifications occurring in the equilibrium of the functions of organism subjected either merely to the action of certain drugs (1) (2), or only to the action of high altitude hypobarism (1), or to the combined action of a drug (strychnine) and of hypobarism (5).

In the present investigation we propose to study the behaviour of the tonus of the iris musculature in the animal ocularly instilled with myotics, in conditions of normal atmospheric pressure and comparatively in the animal with medicinal myosis in conditions of high altitude hypobarism.

Establishing the behaviour of the pupillar diameter in these circumstances is useful for determining the action mechanism of myotics during high altitude hypobarism, and, at the same time, for eventual therapeutical suggestions which might offer valuable indications for aviation medicine.

RESEARCH METHODS

The research was first carried out at normal atmospheric pressure, on the ground, and then at high altitude atmospheric pressure in the barochamber, for being able to appreciate correctly, and comparatively the pupillar modifications of the organism with medicinal myosis in conditions of normal atmospheric pressure, as against conditions of high altitude hypobarism.

1° *Myosis in conditions of normal atmospheric pressure*

The action of myosis on the test animal (rabbit) has been carried out by the monocular instillation, in the right eye (O.D.), of one drop of 1% eserine and 1% pilocarpine solutions, the left eye (O.S.) serving as control.

The pupillar diameter was measured in the following way: in the rabbit placed on the observation table, always identically illuminated, the eyes exposed to an invariable luminous source, situated medianly at the extremity of the nose, from below upwards, the pupillary diameter was measured with a metallic blade, millimetrically

graduated superposed parallelly to the pupillar plane, and as near as possible to the eye — since the eye of the rabbit is oval having a vertical great axis, — for commodity sake we have always measured its diameter horizontally

2° Myosis in conditions of high altitude hypobarism

In general the rabbit was left free in the barochamber, in order to observe its general behavior and at the same time, and within possibilities, the pupillar one However the animal was sometimes immobilized without fastening its head so as to follow bilaterally, the pupillary modifications Other times, the rabbit was immobilized with the head secured in flexion to the right or left resting on the transparent window of the barochamber, for measuring precisely the modifications of the pupillary diameter

The rabbits with medicinal monolateral myosis have been subjected to very high ascents between 8 000 and 12 000 m, corresponding to atmospheric pressures between 267 and 145 mm Hg The ascent to 8 000 m has taken 1 min 50 sec, and the return 40 sec the ascent to 9 000 m 2 min 5 sec and the return 40 sec the ascent to 10 000 m 2 min 24 sec and the return 44 sec the ascent to 11 000 m 2 min 40 sec, and the return 48 sec and the ascent to 12 000 m has taken 2 min 28 sec and the return to the ground 53 sec

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A total of 52 ascents were carried out with 12 animals in a state of myosis Sometimes the same animal, in a state of myosis was subjected at the same sitting to 5 to 9 ascents, while in an interval of 4 to 8 days in another 3 sittings to a total of 11 ascents

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THE RESULT OF RESEARCHES

I Myosis in conditions of normal atmospheric pressure

1st Experiment One drop of 1% eserine is instilled The pupil decreases gradually from its normal horizontal, slightly inconstant and around 5 mm. variable diameter to a constant horizontal diameter of

2 mm Medicinal myosis sets in in 7 min in the restful rabbit and in 10 min in the restless one In this situation, the reactional promptitude of the photo motor reflex myosis decreases gradually to its minimum perceptibility, which appears 15 min after the setting in of the respective maximum myosis produced in 7 or 10 min , after this, the inducing of the photo motor reflex myosis diminishes the pupil to a 1 mm diameter, while the interruption of the luminous stimulus brings the pupil immediately back to the previous 2 mm diameter

2nd Experiment One drop of 1% pilocarpine is instilled monocularly The pupil is gradually reduced from its normal, horizontal diameter, slightly inconstant and variable around 5 mm , to a constant and invariable, horizontal diameter of 4 mm Medicinal myosis sets in in *7 min in the restful rabbit, and in 10 min in the restless one* In this situation, the reactional promptitude of the photo motor reflex myosis diminishes gradually to its minimum perceptibility, which appears after 26 min from the setting in of the respective maximum *myosis,* produced in 7 or 10 min , thereafter, the inducing of the photo motor reflex myosis diminishes the pupil to a 3 mm diameter, while the interruption of the luminous excitation brings the pupil immediately back to the previous diameter of 4 mm

N B In both experiments, the pupil of the opposite eye reacts, all this time, normally Thus, its normal horizontal diameter, slightly inconstant and variable around 5 mm , is modified simultaneously with the inducing of the photo motor reflex myosis, to a horizontal, inconstant diameter, varying around 4 mm The interruption *of the luminous excitation brings the pupil immediately back* to its normal, slightly inconstant diameter, varying around 5 mm

2° *Myosis in conditions of high altitude hypobarism*

The researches carried out in conditions of fictitious high altitude hypobarism in the barochamber, with a monolateral instillation of 1–2 drops of 1% eserine and pilocarpine solutions, have yielded the following results

1 The 2 mm eserinic myosis is transitorily reversible *during the* more or less accentuated convulsions of the animal, thus, while the pupil of the non instilled eye (O S) was in a maximum 9 mm mydriasis, the pupil of the instilled eye (O D) had 6 mm , when the O S pupil had 8 mm , the O D pupil had 5 mm , when the O S pupil has 7 mm , the O D had 4 mm , and when the O S pupil had 6 mm , the O D had 3 mm Thus, the relations between the dimensions of the pupils, when starting from the ground — O S 5 mm , O D 2 mm — remains unaltered during the subsequent increase in their diameter, maintaining *themselves constantly* by *3 mm smaller in* the instilled eye as against the non instilled one

2 The 4 mm pilocarpine myosis is likewise transitorily reversible during the more or less accentuated convulsions of the animal, thus, when the pupil of the non instilled eye (O S) was in a 9 mm

maximum mydriasis the pupil of the instilled eye (O D) had 8 mm, when the O S pupil was in a 7-8 mm medium mydriasis, the O D pupil had 6-7 mm, and when the O S pupil was in a light mydriasis of 6 mm, the O D had 5 mm Thus the relation between the dimensions of the pupils when starting from the ground — O S 5 mm, and O D 4 mm — remains unaltered during the subsequent increase in their diameter, maintaining themselves constantly with 1 mm smaller in the instilled eye as against the non instilled one

3 Medicinal myosis are modified the more rapidly, the more the number of ascents grows, which induce convulsions and finally bring about only generalized muscular quiverings

4 The action of hypobarism, preceding by several minutes the effect of the myotic delays the appearance of myosis in proportion to the altitude to which the animal had been raised

5 The photo-irido motor reflex is absent during maximum mydriasis much delayed during medium mydriasis and slightly delayed in the case of discreet mydriasis in the non instilled eye In the instilled eye however, indifferently of the dimension of the pupil it appears after a long period of latency and is very discreet

INTERPRETATION OF RESEARCHES

1 Myosis in conditions of normal atmospheric pressure

By the inactivation of local cholineresterase and the local favouring of the action of acetylcholine eserine and pilocarpine induces the myosis of the eye on which they had been instilled

The pupillary phenomenon of the parasympathetic type of these two myotic drugs thus set in by the intermediary of a similar action mechanism which is however not identical by the intensity of its manifestation since eserine myosis is more accentuated than the pilocarpine one hence the inference that the favouring of the acetylcholine action is weaker in the case of pilocarpine than in that of eserine

Medicinal myosis occurs more slowly in the restless agitated animal than in the restful, calm one This because the restless animal is in a state of central excitation which has a stimulating effect upon the medullo suprarenal hence the local favouring of the acetylcholine action consequent on the inactivation of cholinesterase, induced by the myotic will be delayed by the transient and repeated action of adrenaline which not only acted upon organism previous to instillation but operates even during the action of the instilled drug and which consists on the one hand in the diminution of the reactivity of the iris cell towards the parasympathomimetic action of acetylcholine and on the other in the freeing of the sympathomimetic reactivation towards the local sympathin. In the calm animal however, in which the acetylcholine generating state of central excita

tion is lacking, it is evident that the action of the myotic will no longer be delayed

If we equate the state of central excitation of the animal which incites its uneasiness, with the state of man's central excitation of a completely special type, which might bring about glaucoma, the above state of facts might thus justify the delayed effect of myotics upon glaucomatous mydriasis In this case the particularly important therapeutical conclusion is that — as shown in the researches of some of us (3), — in the patient's agitated days, myotics cannot fulfill, in ophthalmological clinic, the expected effect, because of the plainly predominant effect of the action of adrenaline *upon the action of* acetylcholine, insufficiently favoured by myotics Therefore, in the very same glaucomatous patient, at the same stage of the complaint, the intraocular action of the myotics varies with the general nervous state of the patient, i e this action is exercised in a curative sense in periods of calm and in a quasi curative or completely non curative sense in the patient's periods of agitation, hence the imperative necessity to associate to the treatment with myotic instillations, that of a general sedative drug

As a matter of fact, Soviet researches come to the support of the conception that adrenaline enters the physiopathological circuit of glaucoma, bringing unquestionable bio chemical evidence regarding the *sympathetic predominance* of the disturbance of the sympathetic — parasympathetic equilibrium *of the nervous* vegetative system in glaucomatous persons Thus Popov's researches (quoted at (6)) have underlined the increase in Ca and adrenaline, and the decrease in K, I and choline in the blood of most glaucomatous patients While Platneva, Raeva and Voronina (quoted at (6)), examining, by Levy's method, the aqueous humour of glaucomatous persons, have emphasized the usual presence of the chemical adrenaline sympathicotropic mediator which raises the activity of the heart and much more seldom that of the vagotropic substance, the acetylcholine, which *lowers the activity of the heart*

The irido motor reflex consists in the constant reduction of the respective pupillary diameter surprised with 1 mm, under the influence of the luminous excitant (eserine 2 mm — 1 mm = 1 mm, pilocarpine 4 mm — 1 mm = 3 mm)

The photo motor myosis or the irido photo motor reflex reaches its minimum perceptibility a very long time after the setting in of the medicinal myosis, namely 45 min after the setting in of eserine myosis and 26 min after that of pilocarpine myosis, which permits the establishing of a directly proportional relation between the intensity of medicinal myosis, undoubtedly connected with the intensity of the local favouring of the action of acetylcholine and the time passed up to the minimum perceptibility in this state of photo motor myosis, i e the more accentuated the medicinal myosis becomes, the longer it takes for the photo irido motor reflex to reach its minimum perceptibility

The veins are particularly affected, although arteries and capillaries are not immune, and characteristically the vasculitis begins at the periphery and may extend backwards even as far as the optic nerve and intracranial vessels (Safar, 1928, Ballantyne and Michaelson, 1937, Verhoeff and Simpson, 1940, Lowenstein and others, 1946) but sometimes the vasculitis may start posteriorly and spread to the periphery Vasculitis thus appears to be the primary change while the capillary irregularities of beading and microaneurysm formation, the recurrent retinal haemorrhages, retinitis proliferans (Fig 3), retinal detachment, glaucoma etc, are all secondary and apparently

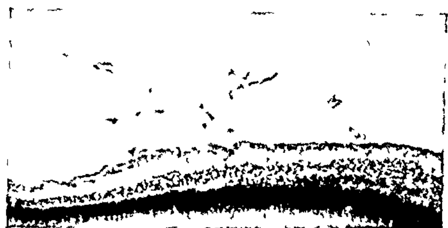


Fig 3 Eales's disease showing new vessels extending into the vitreous from the peripheral retina Haematoxylin and eosin x 112

non specific developments Doden (1960) believes, however, that exudative, proliferative and haemorrhagic forms are clinically quite distinct

A granulomatous reaction is far less frequent than a non specific lymphocytic cuffing In the series reported by Kimura, Carricker and Hogan (1956) twelve eyes showed vasculitis confined to the retinal vessels and in only four of these was the reaction granulomatous In a case of my own, a male aged 40 years with typical Eales's disease the sections showed a patchy granulomatous perivasculitis with giant cells and macrophages, but no causative agent was found (Fig 2)

As already mentioned, an inflammatory reaction may be entirely absent In one interesting case reported by Elliot (1954) (a 24 year old male with typical Eales's disease who died from tuberculous pericarditis only six months after the onset of the eye condition) pathological examination of the eyes revealed no inflammatory process around the vessels, which showed only hyaline thickening Elliot came to the conclusion that these findings were compatible with the theory that the disease had an allergic basis, but it is surprising that the inflammatory reaction disappeared so rapidly

2° Myosis in conditions of high altitude hypobarism

On the ground the local favouring of the action of the acetyl choline by the instilled myotic has a constant character throughout the latter s action

In the barochamber in conditions of high altitude hypobarism, however the respective 2 mm, eserine, and the 4 mm pilocarpine myosis are transitorily reversible and only for the duration of the convulsions of the animal

This means that *the local favouring* of the acetylcholine action by the instilled myotic is subsequently surpassed by the general transitory favouring of the action of adrenaline, subsequent to the passing suprarenalian excitation either directly by anoxious hyperadrenalinaemia or indirectly by the *increased reactivity to* acetylcholine of the higher nervous centres under the influence of hypobarism, whence an important flood of adrenaline, which justifies the maximum mydriasis of the non instilled eye and concomitantly *meanwhile the* tendency of the pupil to return to normal or even the normalization of the pupillary diameter of the instilled eye Thus the fleeting mydriasis *of the non* instilled eye, always synchronous with the proportional increase in the pupillar diameter *of the instilled eye are phenomena* occurring during convulsions determined by hypobarism which by the general favouring of adrenaline hyperproduction mechanisms, act locally upon the iris cell on the one hand, by the diminution of the reactivity of this cell towards the parasympathomimetic action of local acetylcholine — favoured by the instilled myotic — and on the other hand by the freeing of the reactivity of th same cell towards the sympathomimetic action of local sympathin

Thus the degree of *spontaneous* adrenaline mydriasis points out the directly proportional intensity of the degree of the general favouring of the adrenaline hyperproduction mechanisms which act upon the iris in the conditions of the latter s reactivity In other words the iris *not influenced by any instilled drug will always react strictly, proportionally* to the quantity of adrenaline which will arrive on the eyeball But what happens if the reactivity of the iris is influenced by the local parasympathometic action of acetylcholine favoured by the instilled myotic and still more so in the case of eserine than in that of pilocarpine? Then starting from this state of reactivity, the pupillary diameter a result of the two actions (D P R), — the diminution of the iris reactivity towards the *parasympathomimetic* action of local acetylcholine (R i p) favoured by the respective instilled myotic and the liberation of the iris reactivity towards the sympathomimetic *action of* adrenaline arrived on the eyeball (R i s) — will manifest itself by the increase in the diameter of the pupil in medicinal myosis to a new pupillary diameter resulting (D P R) from the pupillary difference (Dif P) between the diameter of the normal pupil (D P n) and the one influenced by the myotic (D P *mio*) a pupillary difference (Dif P) then deducted from the pupillary diameter of the

non instilled eye, mydriatized (D P mid) by hypobarism This situation may be formulated as follows

D P R = R i p — R i s, namely

Dif P = D P n — D P mio, while

Dif P — D P mid = *D P R*, for instance in eserine

Dif P (3 mm) = D P n (5 mm) — D P mio (2 mm)

Dif P (3 mm) — D P mid (9, 8, 7, 6 mm) = D P R (6, 5, 4, 3 mm) pilocarpine

Dif P (1 mm) = D P n (5 mm) — D P mio (4 mm)

Dif P (1 mm) — D P mid (9, 8, 7, 6 mm) = *D P R* (8, 7, 6, 5 mm)

In this case, one may speak of the R i p intensity directly connected to the respective myotic, since the subsequent pupillary modifications under the adrenogenous influence of hypobarism occur from this reactional level

The same adrenogenous influence of hypobarism explains the delay in the action of the myotic, exercised synchronically with the conditions of high altitude

The photo irido motor reflex of the instilled and non instilled eye, manifests itself in relation both with the intensity of the surprised iris contraction, as well as with the type of predominant iris contraction, either parasympathetically, agonistic in the first case, or sympathetically antagonistic in the second case, therefore in the instilled eye the reflex manifests itself very discreetly and only after a long period of latency, while in the non instilled eye, the reflex which is abolished in maximum adrenaline mydriasis manifests itself much delayed in medium mydriasis, and slightly delayed in discreet mydriasis

CONCLUSIONS

Eserine myosis is more intensive than the pilocarpine, since the favouring of the acetylcholinic action is stronger in the case of eserine than in the case of pilocarpine

Myosis appears slower in the restless animal than in the restful one, a fact which signifies that the first is in a state of central excitation, which has a stimulating effect upon the suprarenal glands, while the second, not being in a state of central excitation, thus not stimulating the suprarenal glands to liberate adrenaline, the favouring of the acetylcholinic action of the myotic is no longer delayed

The irido photo motor reflex always diminishes by 1 mm both the normal pupil and the pupil in the respective medicinal myosis hence the significance that the iris excitability threshold is unchanged towards luminous excitation

The fact that irido photo motor myosis reaches its minimum perceptibility a very long time from the complete setting in of myosis

shows that this very long time must elapse from the setting in of medicinal myosis until the final functional influencing of the iris cell by the action of the myotic

In conditions of high altitude hypobarism, the general favouring of the mechanisms of adrenaline hyperproduction takes place, which, at the level of the eyeball, liberating the iris rectivity towards the sympathomimetic action of adrenaline, modifies the medicinal myosis The increase in the pupillary diameter in medicinal myosis, represents, therefore, the resultant of the two local actions the parasympathetic and the sympathetic, in which the latter, favoured by adrenaline predominate, but the parasympathetic action hinders, all the same, a mydriasis identical with the one of the non instilled eye therefore without any parasympathetic favouring and in which pupillary modification will be the sole result of sympathetic favouring

Adrenalinogenous acting of hypobarism justifies on the one hand, the delay in the action of the myotic instilled simultaneously with the subjection of the animal to conditions of high altitude

The irido photo motor reflex depends in its manifestation both on the intensity of the surprised irian contracture, and on the predominant iris contraction time, either agonistically or antagonistically to the photo motor myosis

The Laboratory for Clinical and Experimental Physiology and Physiopathology of the Eye of the Normal and Pathological Physiology Institute Daniel Danielopolu of the Academy of the Rumanian People's Republic Director of the Institute Academician Prof Dr Gr Benetato

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SYMPOSIUM V

CLINICAL ELECTRORETINOGRAPHY

FREQUENCY ANALYSIS OF THE ELECTRORETINOGRAM*

(A preliminary report)

W BEST AND R REUTER

(Univ Augenklinik Bonn Germany), Direktor Prof Dr H K Muller)

When we are faced with an electroretinogram (ERG) we are accustomed to measure amplitude, to look for polarity, whether there is an a, b or x wave, waveletts or an off effect Perhaps we measure latency and other times We were not too much interested in frequency till now and that is also an essential characteristic of an electric potential

We started our investigations at first only to know, what the frequency range of the apparature must be, to get an undisturbed ERG The results of this work we will publish in another paper In this connection it is only of interest that a low frequency filter pass which cuts down all frequencies over 200 cps, has no visible influence on the ERG

Afterwards we became really interested, which frequencies it are which build up the ERG Therefore we tried to make a frequency analysis Many of you when they hear frequency analysis will think at the work of GRANIT and WIRTH and HENKES and coworkers, who used frequency analysis in connection with flicker Our problem is quite another one We want to know, which frequencies are in a single ERG

One can do a mathematical frequency analysis or a physical one With single curves mathematical frequency analysis is rather difficult especially the first part of the curve is not to analyse as far as I know We choose an electric way for analysis For that purpose it is necessary to reproduce the same ERG many times and therefore one has to store it One can store such a potential continuous—that is the analogue method for example with a tape recorder or one can do it in steps —that is the digital method for example with the most computers The latter method is used by JACOBSON and TAKASHI The computer has the advantage that the possibilities for disturbances of the curve are more or less because it works only with on off responses On the other hand there are always steps and there must be many steps to get a result as continuous like with an analogue method

We registered the ERG on a tape recorder That is rather difficult to do Some of you will know that a sufficient direct transformation

* This work was supported by a grant from Deutsche Forschungsgemeinschaft

The frequencies in the ERG seem to be a special harmonic row Perhaps that means, that the high intensity FRG is an overloaded system and therefore there are harmonics One has to bear in mind, that our analysis deals with the ERG we register and there is no simple conclusion to that, what originates in the retina

We wanted to give only a preliminary report Before saying more we need more experiments

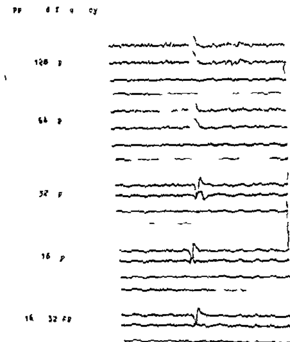


Fig 1 High Intensity ERG (white light 10 000 asb visual field 110) in dark adapted human eye In the five records the upper beam is for comparison in the lower beam the special frequency is suppressed For further explanation see text

REFERENCE

Granit R and Wirth 1953 *J Physiol* 122 386

Henkes, H E. Van der Tweel L H and Denier van der Gon J J 1956 *Ophthalmologica* 132 140

Jacobson J H and Takashi S 1962 XIX *Int Congr Ophth. New Delhi*

Armington J C Tepas D I Kropfl W J and W H Hengst 1961 J opt. Soc Amer 51 877

of slow potential changes on a tape recorder is technically impossible One has to modulate the ERG on a carrier frequency This modulation can be a frequency modulation or an amplitude modulation Armington and coworkers used for their investigation frequency modulation and it may well be, that is the better way, in the meantime there exist several commercial tape recorders, which work with frequency modulation We ourselves used amplitude modulation At first we were rather disappointed to see what came out Little inhomogenities and failures in the magnetic film of the tape caused what is called "drop outs" These drop outs modulate the carrier frequency in the same manner like the signal and disturb the curve seriously We tried many ways and finally we are rather content now We go direct coupled with push pull through our whole apparatus That means we give two modulated carriers in our tape recorder and the drop outs compensate each other The upper limit of frequency range of our whole apparatus is 330 cps This is well over the limit of frequency range, which is necessary to get an undisturbed ERG

With the frequency analysis we started only in the last time We used phase shift amplifiers working with r c networks and Wien bridges with a negative feed back Unfortunately our most filters were at the input condensator coupled So we have a lack in our analysis for the lowest frequencies With 5 cps we had a loss of 50%, with 7 cps of 30% We are on the way to change that

Till now we have analysed only one state of ERG We choose a high intensity ERG of the dark adapted human eye Now to the result We have the impression, that there are some frequencies, which dominate in the ERG In figure 1 these dominating frequencies are suppressed Our filters are not so small, that we can suppress only one frequency and the neighbourhood is in no way altered Therefore we can only say, that we found minimums with that special frequencies But from the many pictures we saw, when we played with our filters and the ERG we had the strong impression, that there are single dominating sinus waves The figure shows five records In the lower three ones we used in addition to the special suppressed frequency a low frequency filter pass with an upper limit of about 50 cps We did that, because in these records we were not interested in the higher frequencies The upper beam shows always an ERG for comparison and in the lower beam the special frequency is suppressed The third beam is for time and photocell registration but that is one of our child diseases, it did not work well

When the frequency of 128 cps is suppressed there are no more wavelets With 64 cps also something happens The curve flattens a little and perhaps therefore some of the wavelets are better to see, than in the original curve The frequencies, which seem to be the most prominent, are 32 and 16 But we should not forget, that these filters are condensator coupled and therefore there is a lack in the low frequencies We had the impression, that between 7 and 10 there is a frequency, which has some influence and there may be lower ones too

Other changes to be found in Eales's disease are a marked thicken ng of the inner limiting membrane (Guyton and Reese, 1948), which was very pronounced in one of my own cases (Fig 4), retinal gliosis,

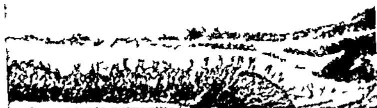


Fig 4 Peripheral retina from a case of Eales's disease Note the extreme thickening of the internal limiting membrane and the haemorrhages into the vitreous Mallory triple stain x 112

and capillary obliteration as may be seen in injected specimens (Fig 5) which occurs especially in those areas where the intravitreal new vessels form (Fig 6) being stimulated by the local anoxia rather than the haemorrhages (Ashton 1957) There may be organising thrombi in the retinal veins which may subsequently disappear entirely in a fibrotic gliosing scar and occasionally the endothelial cells of the vessels may proliferate into the lumen as also occurs in venous thrombosis generally (Fig 7) (Kimura et al 1956) The pronounced hyaline thickening of the vessels is well seen in cross sections and pigment containing macrophages often surround them in sharply localised areas (Fig 8)



Fig 5 Eales's disease Peripheral retina showing extensive capillary obliteration and beading of the patent vessels. Injected Indian ink x 35



Fig 6 Eales's disease showing peripheral neovascularization Note that it arises in an area of capillary obliteration Injected Indian ink x 18



Fig 7 Endothelial proliferation in a retinal vein in a case of central venous thrombosis Haematoxylin and eosin x 190

The frequencies in the ERG seem to be a special harmonic row Perhaps that means that the high intensity ERG is an overloaded system and therefore there are harmonics One has to bear in mind, that our analysis deals with the ERG we register and there is no simple conclusion to that what originates in the retina

We wanted to give only a preliminary report Before saying more we need more experiments

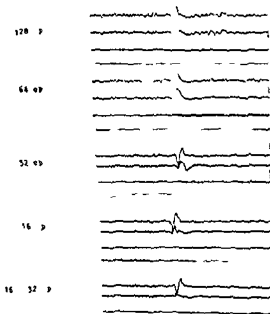


Fig 1 High Intensity ERG (white light 10 000 asb visual field 110) in dark adapted *human eye* In the five records the upper beam is for comparison in the lower *beam* the special frequency is suppressed For further explanation see text

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CHANGEMENTS ELECTRORETINOGRAPHIQUES A L'ETAT HYPNOTIQUE

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I

Dans l'etude de l'hypnose comme phenomène physiologique il y a une forte tendence d'etudier ce problème par des methodes experimentales objectives. Nous nous sommes mis comme devoir partiel d'examiner l'influence des changements fonctionels du systeme nerveux central pendant l'hypnose sur les faits bioelectriques dans la peripherie de l'analysateur visuel dans la retine.

La personne examinee etait adapte pendant 5 minutes a une illumination de 25 lx. Le stimulateur était un eclair electronique a une periode de stimulation de 0,002 seconde a peu pres. Nous avons repete regulièrement les stimulus lumineux toujours apres 15,20, eventuellement 30 secondes. Nous avons faits chaque fois une serie d'ERG photopiques au cours de l'hypnose et apres le reveil. Nous avons ainsi etabli 8 series d'ERG dans 7 personnes agées de 24 a 48 ans. Avant l'hypnose nous avons faits 171 ERG evaluables, pendant l'hypnose 167 et apres le reveil 113 ERG. Afin d'empecher la paupiere superieure de tomber pendant l'hypnose, nous avons appliqué a l'oeil droit un blepharostat pour assurer ainsi qu'une quantité constante de lumiere tombe sur la retine. L'oeil gauche etait sans blepharostat et d'apres l'abaissement de la paupiere superieure nous avons evalue le debut de l'hypnose.

L'hypnose etait provoque par suggestion verbale, pour la fixation visuelle nous nous sommes servi des contours de la lampe du photostimulateur. Nous avons choisi pour l'examen des personnes qui etaient deja auparavant hypnotisees et entraient facilement dans l'état hypnotique moyen, l'hypotaxie. Les personnes examinees appartenaient du point de vue diagnostique dans le group de nevroses eventuellement des personalités psychopathiques avec des difficultes neurotiques.

II

Les changement dans ERG au cours de l hypnose etaient determines sur des series d ERG dans deux personnes sur les parametres suivants

1 Une diminution du potentiel de l onde a

2 Une augmentation ou diminution du potentiel d l onde b

3 Prolongement du temps du parcours de l onde b

Dans les autres 5 personnes les constatations de l ERG au cours de l hypnose étaient moins exprimees ou ne pouvaient pas etre prouvees statistiquement Dans ces personnes examinées on n arrivait pas a un degré d hypno e aussi grand que dans des personnes dont les constatations etaient statistiquement changées

III

La plupart des rechercheurs dans la domaine de l hypnose considérent l etat hypnotique comme un fait du centre nerveux Aussi dans l analysateur visuel la suppression hypnotique se fait surtant dans les regions centrales Chez les personnes examinees avec une constatation positive une interruption du contact visual avec les environs a eu lieu Ils disaient que parfois ils ne concevaient par les eclairs *repété de la lumière* Dans la litterature sont decrits des troubles de vue pendant l hypnose qui se produisaient spontanement sans *suggestion* speciale(Doelken' En 1956 Vanysek s occupait des *rapports e tre le* systeme nerveux central et l adaptation de la *retine au crepuscule* que se traduisait sur l electroretinogramme par une baisse de l onde a après une suggestion verbale de l imagination d un *éblouissement* La question d un reflet centrifuge des fonctions centrales dans la *périphene* de l analysateur interessait déjà I M Setchenoff qui *maintenait que la* perception est un anchainement reflecteur complique E N *Sokolov* juge qu en dehors de la fonction centripétale au *cours de la perception* generalement admis existe aussi un fait contraire *passant du centre* vers la périphene Il s agit ici d un *complement reversible* l autoregulation dont un exemple est la *photoreaction des pupilles* l influence du centre sur la formation du pourpre visuel et autres

Kozousek et Vanysek presument a la base des etudes antérieures que dans le rapport de la *retine avec la* partie centrale de l analysateur il existe trois types basales *de la regulation* deja connus dans la sciences naturelles Ils peuvent etre exprimes par *des formules* et des connections schematiques Le plus bas degre c est la regulation proportionelle le plus haut degré la régulation *dérivatoire et intégrale* Dans la rétine se font valoir tous les trois sortes *de regulation* Les centres cérébraux reglent le complément reversible qui se fait valoir directement dans la retine

groupement statistique		*potentiel de l onde a en mm*	*potentiel de l onde a en μv*	*potentiel de l onde b en mm*	*potentiel de l onde b en μv*	*periode de la tence en mm*	*periode de la tence en sec*	*passage temporel de l onde b en mm*	*passage temporel de l onde b en sec*	*potent de l onde a en mm*	*potent de l onde a en μv*	*potent de l onde b en mm*	*potent de l onde b en μv*
A	moyenne arithmetique	6 0	120	7 4	144	1 26	0 021	2 1	0,035	5,8	99	9,35	159
avant l hypnose	deviation decisive	0 96		1 0		0 22		0 28		0 83		0 61	
B	moyenne arithmetique	2 1	42	9 9	193	0 82	0 014	3 3	0 035	5 5	93	6 77	116
pendant l hypnose	deviation decisive	1 4		1 0		0 80		0 75		0 72		1 03	
C	moyenne arithmetique	7 4	148	5 7	111							7 4	127
peu de temps après le réveil	deviation decisive	1 37		1 07									
groupement statistique	déviation decisive de la difference	0 34		0 46		0 26		0 25				0 27	
A B	test	11 3		5 44		1 69		4 8				9 53	
groupement statistique	deviation decisive de la difference	0 51		0 43									
A C	test	2 8		3 96									

CONCLUSION

Les constatations que nous venons d ecrire montrent que l etat inhibitif du cerveau peut avoir une infuence considérable sur le cours de potentiels de la retine qui peut etre considere comme une autre preuve de l activite regulatoire du fonctionement cerebral sur le fonctionement de la retine

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groupement statistique		potentiel de l'onde a en mm	potentiel de l'onde a en µv	potentiel de l'onde b en mm	potentiel de l'onde b en µv	periode de latence en mm	periode de latence en sec	passage temporel de l'onde b en mm	passage temporel de l'onde b en sec	potent de l'onde a en mm	potent de l'onde a en µv	potent de l'onde b en mm	potent de l'onde b en µv
A	moyenne arithmetique	6,0	120	7,4	144	1,26	0,021	2,1	0,035	5,8	99	9,35	159
avant l'hypnose	déviation decisive	0,96		1,0		0,22		0,28		0,85		0,61	
B	moyenne arithmetique	2,1	42	9,9	193	0,82	0,014	3,3	0,055	5,5	93	6,77	116
pendant l'hypnose	deviation decisive	1,4		1,0		0,80		0,75		0,72		1,03	
C	moyenne arithmetique	7,4	148	5,7	111							7,4	127
peu de temps après le réveil	deviation decisive	1,37		1,07									
groupement statistique	deviation decisive de la difference	0,34		0,46		0,26		0,25				0,27	
A B	test	11,3		5,44		1,69		4,8				9,55	
groupement statistique	deviation décisive de la difference	0,51		0,43									
A C	test	2,8		3,96									

All patients of the group receiving cystein (electrophoresis 3–5 per cent solution) have displayed temporary increase of visual function

In four patients FRG appeared immediately after the administration of cystein and gradual further abolishment of ERG

ON THE REGISTRATION OF ELECTRICAL PROCESSES IN THE ISOLATED RETINA AND THE OPTIC NERVE IN COLD BLOODED ANIMALS MAMMALS AND MAN

DEMIRTCHOGLIAN G G ALIAHVERDIAN M A BLAVATSKAYA L D and MIRZA AVAKIAN I I (*USSR*)

The investigations of the Physiological Institute of the University of Leipzig have shown that the isolated retina washed in the cultural solution (modified Tirode Solution or Plasma) can be used for the study of the role of metabolic processes in the generation of the ERG

In the paper of W Sickel and G Demirtchoglian (1961) the role of the SH groups in the origin of the ERG of the frog has been shown and the ERG of the isolated retina of man was recorded

In our laboratory investigations have been made on the study of the light and dark adapted isolated frog retina and optic nerve The off effect of the total discharge of the optic nerve increased significantly and the on effect decreased after the light adaptation This could be repeated many times provided the preparation is in a good functional state (the preparation has been active during two days)

In mammals enucleation of the eye and a part of the optic nerve has also been performed The isolated retina and the optic nerve were washed with a warm plasma The electrical reaction has been recorded by microelectrodes and cathode ray oscillograph with a d c amplifier The FRG and the electrical activity of the optic nerve were recorded during 3–4 hours Various chemical effects of substances used in ophthalmology were also studied

In three patients the eye was enucleated and the ERG of the isolated retina was recorded after washing with a warm and fresh plasma during 4–6 hours The FRG consisted of the a and b waves the d wave was absent

The microelectrode recording permitted us to discover the FRG of the different layers of the isolated retina of man

THE MOLECULAR BASIS OF THE ORIGIN OF THE ERG OF ANIMALS AND MAN

DEMIRTCHOGLIAN, G G (*USSR*)

In our investigations great attention has been paid to the determination of the role of SH groups of light sensitivity and other protein substances of the retina in primary visual processes and ERG in the normal and other pathological states

The important role of the SH groups in the nature of primary visual processes and the metastable state of light sensitive molecules served as an initial theoretical assumption (Demirtchoglian, 1950)

The importance of the SH groups in the development of photo chemical processes in rhodopsin was shown, as it is known (Wald & Brown, 1951)

Later, it was shown in our laboratory that the change of retinal function (ERG) after the action of ionized radiation may be connected with the decrease of the amount of SH groups in the retinal homogenates (Ohanjanian, V G , 1959)

More direct information has been received on the role of the SH groups in the origin of ERG at the Physiological Institute of Leipzig (W Sickel and G Demirtchoglian, 1961)

The preparation isolated from the retina of the frog, mammals or man was placed in a chamber with electrodes and washed by a cultural solution (modified Tirode solution or plasma), the addition of mercury containing substances (uragan 10^{-6} or 10^{-5} M) has led to the rapid extinction of the ERG Light adapted retina was more sensitive to the blockade of SH group than the dark adapted one

After adding cystein (10^{-4} or 10^{-5} M) to the cultural medium the complete recovery of ERG and its spectral sensitivity was obtained Cystein has also shown protected effect when the SH group of the retina was blockaded

In experiments of the normal isolated retina of man it was discovered that by adding uragan (10^{-5} M) to the plasma no effect of ERG extinction was noticed The action of cystein had little effect (10^{-4} M)

From the data received and the capability of cystein to preserve *the retina* of the rabbit from the development of pigment degeneration (*Sorsby* and Harding, 1960) *experiments were* made on the study of cystein action on the retina of patients with retinitis pigmentosa (G G Demirtchoglian, I Blavatskaya, J Mirza Avakian, S Gevorkian, 1961)

detecting at a clinically benign stage those cases which will go on to malignant stage and carry a distinctly poorer prognosis before retinopathy has become clinically apparent or gross bio chemical changes in blood have taken place

It is surprising that with so much of fundamental background known to the physicians the physiologists and the ophthalmologists and so much of clinical material abundantly available in all clinics the utility of electro retinography has not been adequately exploited in the assessment of prognosis in Systemic Vascular Hypertension

This report is based on a study of 96 cases of essential hypertension 63 of which could be followed up for upto 2 years after the first record In the control series of comparable age groups the average b potential was 0.30 mV the response was sub normal in 29% and normal or super normal in 71% cases A response of .25 to .35 mV is therefore considered a normal range Potential below .25 mV is treated as sub normal and above .35 mV as super normal

It should however be made clear that ERG records of this study are qualitative in nature and not of quantitative accuracy It is based on electro retinography by Karpes initial method with five minutes dark adaptation, 80 lux illumination stimulus of ½ sec repeated at 15 sec interval and the potential recorded on an electro cardiograph with an amplification of 1 mV on 1 cm It can therefore at best be expected that these observations open out a field of more intricate studies in clinics where more advanced and sensitive electronic equipment facilities are available

Hypertensive cases were mostly in the age group of 30 to 70 years and only 7 cases were between 18 to 25 years and five older than 70 years

The following table I summarises the electrical response of the retina in relation to the grade of retinopathy and average blood pressure

TABLE I

Grade of Retinopathy	*No of Cases*	*Average Blood pressure*	*Average b-potential*			
			Normal or Super normal		*Sub normal or Extinguished*	
			No	%	No	%
Grade I	6	176/109	12	43.0%	14	57.0%
Grade II	33	190/124	16	48.5%	17	51.5%
Grade III	18	217/123	8	44.5%	10	55.5%
Grade IV	19	233/134	5	26.3%	14	74.7

ELECTRO RETINOGRAPHY IN SYSTEMIC VASCULAR HYPERTENSION

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Not foreseeing the future victims of radiation, 30% of deaths after the adult age are of vascular origin whether cardio-vascular, cerebro vascular or vasculo vascular Whether as a consequence or as a basic cause, clinical hypertension is a subject attracting more and more attention Therefore every medical consultant is interested in being able to pre judge the further progress and prognosis of an individual case There are cases who have lived a full span of life consistent with hypertension while there are numerous others who though start as innocuously have their fate sealed within a few months to a few years Efforts at assessing a prognosis are still limited to blood bio chemistry and grading of retionopathy If a person's blood urea is markedly raised and his retinopathy is in grade IV, no insurance company will cover him as a risk, and the journey before the patient is so short and fast that hardly can he think and plan

After all, every case of hypertension starts as a simple case and it is therefore pertinent that one would if possible like to sort out hyper tension at a much earlier stage and to decide as to which particular case is likely to go on to malignancy and which particular case will be compatible with full span of life

Retinal function is directly dependant upon the vascular nutrition it receives Any metabolic or nutritional disturbance is likely to be manifest as a functional deficiency even tho gh it may be sub clinical Good visual acuity full field of vision and normal ophthalmoscopic findings are consistent with a retina which may be functioning under certain handicap for example Vitamin A content of plasma must fall from a normal level of 98 to 192 100 c c to as low as 30 international unit/100 c c before clinical night blindness may become manifest

Blood circulation in the eye being of the decisive importance for the type and shape of electro retinogram, systemic vascular hypertension associated with arterial attenuation and consequent subclinical anaemic condition of retina may result even though clinically and anatomically structures appear normal It should therefore, be a live possibility that electro retinographic studies in hypertension may possibly help in

The veins are particularly affected, although arteries and capillaries are not immune, and characteristically the vasculitis begins at the periphery and may extend backwards even as far as the optic nerve and intracranial vessels (Safar, 1928, Ballantyne and Michaelson, 1937, Verhoeff and Simpson, 1940, Lowenstein and others, 1946) but sometimes the vasculitis may start posteriorly and spread to the periphery Vasculitis thus appears to be the primary change while the capillary irregularities of beading and microaneurysm formation, the recurrent retinal haemorrhages, retinitis proliferans (Fig 3), retinal detachment, glaucoma etc , are all secondary and apparently



FIG 3 Eales s disease showing new vessels extending into the vitreous from the peripheral retina Haematoxylin and eosin × 112

non specific developments Doden (1960) believes, however, that exudative, proliferative and haemorrhagic forms are clinically quite distinct

A granulomatous reaction is far less frequent than a non specific lymphocytic cuffing In the series reported by Kimura, Carricker and Hogan (1956) twelve eyes showed vasculitis confined to the retinal vessels and in only four of these was the reaction granulomatous In a case of my own, a male aged 40 years with typical Eales's disease the sections showed a patchy granulomatous perivasculitis with giant cells and macrophages, but no causative agent was found (Fig 2)

As already mentioned, an inflammatory reaction may be entirely absent In one interesting case reported by Elliot (1954) (a 24 year old male with typical Eales's disease who died from tuberculous pericarditis only six months after the onset of the eye condition) pathological examination of the eyes revealed no inflammatory process around the vessels, which showed only hyaline thickening Elliot came to the conclusion that these findings were compatible with the theory that the disease had an allergic basis, but it is surprising that the inflammatory reaction disappeared so rapidly

detecting at a clinically benign stage those cases which will go on to malignant stage and carry a distinctly poorer prognosis before retino pathy has become clinically apparent or gross bio chemical changes in blood have taken place

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This report is based on a study of 96 cases of essential hyperten sion 63 of which could be followed up for upto 2 years after the first record In the control series of comparable age groups the average b potential was 0 30 mV the response was sub normal in 29% and normal or super normal in 71% cases A response of 25 to 35 mV is therefore considered a normal range Potential below 25 mV is treated as sub normal and above 35 mV as super normal

It should however be made clear that ERG records of this study are qualitative in nature and not of quantitative accuracy It is based on electro retinography by Karpes initial method with five minutes dark adaptation 80 lux illumination stimulus of ¼ sec repeated at 15 sec interval and the potential recorded on an electro cardiograph with an amplification of 1 mV on 1 cm It can therefore at best be expected that these observations open out a field of more intricate studies in clinics where more advanced and sensitive electronic equipment facili ties are available

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TABLE I

Grade of Retinopathy	No of Cases	Average Blood pressure	Average b-potential			
			Normal or Super normal		Sub-normal or Extinguished	
			No	%	No	%
Grade I	26	1 6 109	12	43 0	14	57 0%
Grade II	33	1 0/1 4	16	48 5%	17	51 5%
Grade III	18	217/123	8	44 5%	10	55 5%
Grade IV	19	223 134	5	26 3%	14	74 7%

It will be appreciated from this table that 51.5 to 57% cases have a sub normal ERG which is distinctly higher than the normal percentage. It is however still significant to note that the percentage of sub normal response suddenly increased to 74.7% in grade IV retinopathy. It will also be noted that this increase in subnormal response is also proportionate to the increase in blood pressure. It is therefore suggested that the electrical retinal potential may have a direct relationship to the grade of retinopathy and the severity of hypertension.

Again table II below co-relates the retinal response to systolic, diastolic and pulse pressure.

TABLE II

		No. of cases	Normal or Super normal		Sub-normal or Extinguished	
			No	%	No	%
Systolic	150–199	47	24	53.2%	23	46.8%
	200–250	40	14	35.0%	26	65.0%
	Over 250	9	2	22.5%	7	77.5%
Diastolic	95–124	62	26	42.0%	36	58.0%
	125–150	29	12	41.4%	17	58.6%
	Over 150	5	1	20.0%	4	80.0%
Pulse Pressure	30–74	48	25	52.0%	23	48.0%
	75–100	34	12	35.3%	22	64.7%
	Over 100	14	3	21.5%	11	78.5%

It is again significant to note that the percentage of sub normal response is directly proportional to the increase in systolic, diastolic and pulse pressure.

In the same way the following table III is an attempt of co-relating the b potential to the prognosis of hypertension.

TABLE III — *Follow-up in Relation to b Potential*

	No. of Cases	Super normal or normal		Sub normal or Extinguished	
		No	%	No	%
Improved	28	15	53.5%	13	64.5%
No Improvement	15	5	33.3%	10	66.6%
Died	20	6	30.0%	14	70.0%

These observations equally strictly support the earlier suggestion in a follow up of 63 cases which could be dependably followed up for 2 years Of 28, which continued to improve with treatment only 46 5% had a subnormal response 66 0% were subnormal in those 15 which did not respond to therapy The percentage of subnormal response was 70 0% in those 20 cases who later died within 2 years of the follow up period A *subnormal response* thus is again suggestive of the seriousness of the prognosis of Essential Hypertension

These observations are further supported by a few individual case records

Case I—M 76 G B 36 yrs F B P on admission 165/110 Bl Urea 22 mg % Retinopathy grade I First ERG on 4 5 60 Av b pot 252mV Clinical condition improved with hypotensive drugs ERG repeated 9½ months later The electrical potential improved to 45mV During a follow up of upto May 1962, the patient was under control and asymptomatic The initial nearly normal response and an increase of b-potential later supported by clinical observations is indicative of good prognosis and the benign nature of hypertension

Case II—M 64 G 40 yrs M, Admitted with B P 220/140 and Bl Urea 24 mg % Retinopathy grade I First ERG on 23 3 60 Av b pot 282mV As the patient was not improving with treatment ERG repeated 7 weeks after the first one and the b pot recorded was 132mV Patient ultimately died 10 days later The b pot although normal in the initial stage, rapidly becoming subnormal and the patient dying soon after is suggestive of poor prognosis, even though biochemistry and the grade of retinopathy were not indicative of the seriousness of the disease

Case III—M 56 B L 47 yrs M Admitted with B P 260/150 Bl Urea 45 mg % and Retinopathy grade III ERG recorded on 15 3 60 Av b-pot 112mV Patient died 15 days later A markedly subnormal ERG in this case further supports the seriousness of the condition indicated by higher blood urea and retinopathy

Case II—B-40 H L 25 yrs M Admitted with B P 184/122, Bl Urea 10 mg % but Retinopathy clinically looking grade IV First ERG on 15 3 57 Av b-pot 275mV Patient clinically improved with treatment and the Av b pot recorded 9 months later b-pot improved to 425mV Follow up indicated that the patient was well under control for upto 4 yrs thereafter Although retinopathy indicated the seriousness of the disease but a normal Bl Urea and a normal initial ERG rising still further later on supported by clinical condition

is suggestive that the ERG could be a dependable guide in the prognosis of hypertension and the retinopathy in this case may be due to other factors

Last *Case* I — B & S 52 I B 30 yrs F, Was first admitted with B P 210/140 Bl Urea 22 mg % and retinopathy grade II First ERG recorded on 17-3 57 with Av b pot 165mV Patient responded to treatment and left hospital asymptomatic Patient was readmitted for recurrence of symptoms 1 year later with B P 258/140 and Bl Urea now risen to 80 mg % and retinopathy now grade III Second ERG recorded on 19 3-58 Av b pot 125mV Patient left the hospital against advice after some symptomatic improvement but returned again 3 months later with B P 255/170 Bl Urea mg % and retinopathy now grade IV Av b pot recorded on 21-6-58 was 069mV and the patient died a month later on 21-7-58 In this particular case, if we go back to the findings at first admission 1 year and 4 months before death, neither retinopathy grade II nor Bl Urea 22 mg % was indicative of the seriousness of disease Distinctly sub normal ERG at that stage was the only indication suggestive of oncoming seriousness of the disease which was supported by subsequent findings and the ultimate death

On the basis of these studies, I make the following suggestion —

1 That a subnormal response in a case of clinical hypertension may be suggestive of oncoming malignancy at a later date and therefore should be an unpleasant finding

2 Falling b potential during repeated ERG, is still more indicative of the possibility that a clinically benign hypertension may be the beginning of malignancy

3 ERG may be a fairly dependable means of assessing the prognosis of a particular case of hypertension even at a stage when neither retinopathy nor bio chemistry of blood are a helpful guide

4 ERG should be a routine procedure of investigation in all cases of essential hypertension

USE OF AN AVERAGING COMPUTER IN ANALYSIS OF THE HUMAN ERG

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As investigators have pursued the analysis of the electroretinogram further and further in detail attempting to exact as much information as possible from their records measurement and study of small sub components of the ERG as well as detection of minute responses, have become a problem of increasing interest

Several approaches have been made to increase the ability of our recording and amplifying system to provide the information we are all seeking

If we assume that satisfactory amplifier design is utilized of necessity the limiting factor in such minutious seeking is the recording system

There are several types of recording system in use each with its own advantages and drawbacks We wish to present our experience with one which we consider has several great advantages

The ink writing electroencephalograph machine has one great advantage over all others It is simple foolproof and sturdy For recording of the gross features of the ERG response I believe it is highly satisfactory and still forms the basis of much of our clinical work There are however, several disadvantages to its use Because it is an electromechanical device in which the mass of the pen must be moved there is a definite inertia to the system which induces a loss of the fast portions of the response

This loss of fast response is overcome if a cathode ray oscilloscope is used as the recording device This device by virtue of its minimal distortion since the only inertia is due to the *infinitesimal* mass of the electrons which are the indicator, is much more responsive to fast changes It however required some sort of photographic technique for permanent registration of results and this may result in delay in interpretation of results

In addition since each record may contain a few minute elements of the response or an extremely minute response, it is only by comparison of a large series of such photographs that one can be certain of the presence with regularity of some small sub-component of the response

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In addition since each record may contain a few minute elements of the response or an extremely minute response it is only by comparison of a large series of such photographs that one can be certain of the presence with regularity of some small sub-component of the response

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Last *Case V*— B & S 52 L B 30 yrs F, Was first admitted with B P 240/140 Bl Urea 22 mg % and retinopathy grade II First LRG recorded on 17-3 57 with Av b pot 165mV Patient responded to treatment and left hospital asympto matic Patient was readmitted for recurrence of symptoms 1 year later with B P 258/110 and Bl Urea now risen to 80 mg % and retinopathy now grade III Second ERG recorded on 19 3-58 Av b pot 125mV Patient left the hospital against advice after some sympatomatic improvement but returned again 3 months later with B P 255/170 Bl Urea mg % and retinopathy now grade IV Av b pot recorded on 21 6 58 was 069mV and the patient died a month later on 24-7 58 In this particular case, if we go back to the findings at first admission 1 year and 4 months before death, neither retinopathy grade II nor Bl Urea 22 mg % was indicative of the seriousness of disease Distinctly sub normal LRG at that stage was the only indication suggestive of oncoming seriousness of the disease which was supported by subsequent findings and the ultimate death

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to go off at the time of the 20th memory cell This allows the observation of the base line of activity *prior* to the stimulus As the first *response* is obtained each memory is charged with an amount of potential proportional to the amplitude of the response at its particular moment in time Each following response then adds to the charge in the particular memory at the identical time relative to the stimulus light It is possible to obtain in this manner several hundreds or thousands of responses and to store in the series of memories, the *SUM* of the electrical potential of all of them, at each point in time

The instrument is operated on line , that is directly connected to the patient by way of an amplifying system and *slide* 2, the summed response is visible, as the sum is accumulated, on the face of a cathode ray tube in the panel This on line feature eliminates much of the difficulty found in the use of the tape recording system described above

Since this device is synchronized with the stimulus flash the electrical events which occur at the same time after each will be superimposed and hence reinforced Random eyeball motion, power line and other artifactual electrical noise will not occur at the same time *after each response and such contaminants of our records are statistically* cancelled When the desired number of responses have been recorded one may photograph the face of the CRO tube, or use an X Y recorder or other device to obtain a permanent record

This device has therefore the advantages of allowing us to obtain the sum of a large number of responses and to cancel out *erroneous* factors and we believe hence to achieve our aims of increased fidelity of recording of fast components as well as minute ones

I should like to show you a few examples of what the instrument will do (Slide 3) This is a patient with a retinal degeneration in whom using a standard inkwriting technique—and *incidentally* although not shown on the slide also using a CRO, only a minimal response is demonstrable By summing 100 responses, however, it is possible not only to be sure that the response observed is not an artifact but to observe certain of its characteristic conformations

Slide 4 This slide shows the ability of the device to record the characteristics of fast flickering responses—here up to 80 per second It is to be noted that when the inkwriter records only a smooth sine wave form we are able to *discern* a non sinusoidal pattern

Slide 5 Utilizing this technique following the lead of Heck and Rendahl who first reported using the CRO the presence of small components of the response we were able to confirm their findings as shown on slide 5

The increased fidelity of this technique removes the possibility of these being artifacts Slide 6 shows a comparison of the time relationships obtained by Heck and Rendahl below and by Jacobson and Suzuki above Recently we confirmed some of their findings in colour

Some of this difficulty may be eliminated by the use of multiple exposure tracings, such as *slide* 1 but when a large series of responses are thus recorded, the result may be an incoherent blur

Harold Henkes has advocated another technique for recording of multiple responses using a frequency tuned amplifier but, while this may present evidence of some activity at a particular frequency—and, if this frequency is that of a stimulus light—it may be adduced that there is a response in an eye which had not produced a response of measurable proportion by other techniques The shape of the response is however, grossly distorted by this instrument Recently, we have had access to an averaging computer

This development of electronics has allowed us to pursue the aims of increased fidelity of recording the ERG with a series of new instruments The aims of these techniques are the same two outlined above (1) Increased capacity to measure fast components of the response and (2) Increased capacity to record minimal potentials and minute sub components

Our first approach was the utilization of the tape recorder There exist instruments of this type in which the signal (as we may call the ERG) is allowed to modulate the frequency of a carrier wave, similar to the technique used in FM broadcasting By this technique very accurate records of the potential may be obtained If a series of responses are thus recorded on a length of tape, a device can be utilized which will allow us to make a "closed loop", or endless belt of this tape and play it over and over again through a playback head It is possible then to sample the amplitude of each response at a given PERIOD after the stimulus light flash and to integrate or sum up the amplitude of the response at, let us say 10 milliseconds after the stimulus in each of 100 responses This sum can be permanently recorded and the machine now reset to provide this type of sum at 20 milliseconds after the stimulus response The sums can be drawn sequentially and the total curve of the 100 responses will be obtained

We were deeply involved in this technique, which I regret to say, in our hands at least, was beset with technical problems—when a new instrument became available This device, which is called a "computer of average transients" is basically a series of electronic memories, really, capacitors capable of storing an electrical potential and of releasing this charge at demand into a recording system Each of the 100 such memories in this device is made to correspond to a given instant of time Thus if we choose to study the electrical activity of the eye beginning ten milliseconds before stimulation and to continue to observe the response for a total of one tenth of a second, each of the memories is set to be equivalent to 1/1000 of a second

In use, the memories at the beginning of an experiment are all emptied of charge, and the timing circuit of the device is set so as to provide stimuli at the desired frequency through a *triggering* circuit which controls the stroboscopic light source This flash is usually set

male of 30 years with active pulmonary tuberculosis and bilateral Eales s disease who died six years later after pneumonectomy, the uvea was entirely normal and the filtration angles widely patent Using PAS stain Wagner and Conrads (1959) found changes in the ground substance of the venous walls which they attributed to lytic processes resulting from an antigen antibody reaction

Very few of these changes can be claimed to be specific for Eales s disease yet the whole combine to present a characteristic picture of a chronic low grade grumbling inflammatory reaction with degenerative and proliferative changes

Aetiology

TUBERCULOSIS

The concept that Eales s disease is due to a direct infection of the retinal vessels by tubercle bacilli is not very convincing The history of the evolution of this theory has been traced in detail by Donders (1958) and it is based on four points First upon the undoubted association of Eales s disease with cases of active tuberculosis secondly upon the presence of giant cells and granulation tissue around the vessels, thirdly upon the demonstration of tubercle bacilli in the vicinity of the vessels on four occasions (Gilbert 1914, 1935, Otori 1915 Frank 1925 Stock 1937) and *fourthly* upon the experimental production of retinal periphlebitis by the injection of tubercle bacilli (Finnoff, 1924 a b Uyama, 1936 Meyer 1940) Against this it should be noted that many cases of Eales s disease have been reported where there has been no evidence whatsoever of tuberculous infection a granulomatous reaction, even if tuberculous in appearance can be simulated by other disease entities the finding of tubercle bacilli on so few occasions suggests that these positive cases may belong to a different category probably to miliary tuberculosis (Goldstein and Wexler 1930) while the experimental lesions bear little resemblance to Eales s disease To me it seems inconceivable that infection with tubercle bacilli could give rise to such a restrained and diffuse inflammatory reaction as seen in periphlebitis

There is however good reason to suppose that tuberculosis may play some role in a proportion of cases for the not infrequent association of Eales s disease and active tuberculosis in young individuals appears too striking to be dismissed as a chance occurrence In India for instance Eales s disease has a higher incidence than in Western countries and this has been attributed to a higher incidence of tuberculosis (Gupta 1958)

On theoretical grounds it would seem entirely possible that the retinal vessels may become selectively sensitized to tuberculoprotein and that an allergic vasculitis results when the vessel are again subjected to this antigen Experimentally, animals pre treated with intraocular tuberculin developed retinal vasculitis when tubercle bacilli were later introduced into the circulation (Uyama 1936 Meyer 1940)

THE EFFECTS OF SEROTONIN RESERPINE AND JB-516 ON THE ERG

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Adrenalin and acetylcholine have been studied extensively in the stimulus conduction mechanism of the central nervous system Cathecolamines and serotonin however have been investigated intensively in the same field only in recent years

Twarog Page Brodie and others doing research work of the brain have found out many details about the natural occurrence tissue distribution biosynthesis and many other functions of serotonin

However the significance of serotonin in ophthalmology is almost unknown as yet Its existence in the retina seems to be proved by a histochemical demonstration of the changes in the monoaminoxidase activity that occur in the rabbit retina after the intravenous administration of serotonin according to experiments carried out by Kojima and other collaborators of our department of ophthalmology

Here we report the results of our research work concerning the function of serotonin in the retina from the electroretinographical point of view

MATERIAL METHOD

Albino rabbits on which no general anesthesia was performed and in whose eyes mydriasis was produced by a one per cent atropine solution were dark adapted for half an hour before their ERGs were recorded

The recordings of ERGs extended over a period of about 48 hours and the different effects caused by the various substances injected intravenously were as follows For the light stimulation Buffington s photic stimulator and a contact lens electrode were used The amplitude of the a and b wave were measured compared and studied

RESULTS

1 Effect of serotonin The amplitude of the b wave decreased evidently half an hour after the administration of a relatively large dosage of serotonin 30 mg kg) and this effect continued for about 48 hours A series of subsequent studies with dosages of 20 10 and 5 mg per kg respectively indicated that a dosage of 20 mg or less caused no changes From these facts I suggest that there is a blood retinal barrier for this substance

blind individuals The complete paper dealing with this subject will be published shortly in the AMA Archives of Ophthalmology, but this is a *composite* slide to show some of the alterations of responses obtained in several forms of colour deficiency

Slide 7 shows how effectively this device will screen out sixty cycle artifact from the power lines

To sum up, therefore, we believe that this averaging computer, while certainly not the *ultimate* instrument for recording of the ERG, is, in our opinion, the best yet *available* for observation of fine, fast components of the response Its disadvantages are its cost and the fact that it is a statistical averaging device, which may compromise the characteristics of each of a series of responses, i e , make it possible to determine how the first of a series may vary from the *sequential* ones In order to overcome this objection we routinely record simultaneously with the CRO and the inkwriter, in thus instances where this is important

THE EFFECTS OF SEROTONIN RESERPINE AND JB 516 ON THE ERG

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Adrenalin and acetylcholine have been studied extensively in the stimulus conduction mechanism of the central nervous system Cathecolamines and serotonin, however have been investigated intensively in the same field only in recent years

Twarog Page, Brodie and others doing research work of the brain have found out many details about the natural occurrence tissue distribution biosynthesis and many other functions of serotonin

However, the significance of serotonin in ophthalmology is almost unknown as yet Its existence in the retina seems to be proved by a histochemical demonstration of the changes in the monoaminoxidase activity that occur in the rabbit retina, after the intravenous administration of serotonin according to experiments carried out by Kojima and other collaborators of our department of ophthalmology

Here we report the results of our research work concerning the function of serotonin in the retina from the electroretinographical point of view

MATERIAL METHOD

Albino rabbits on which no general anesthesia was performed and in whose eyes mydriasis was produced by a one per cent atropine solution were dark adapted for half an hour before their ERGs were recorded

The recordings of ERGs extended over a period of about 48 hours and the different effects caused by the various substances injected intravenously were as follows For the light stimulation Buffington s photic stimulator and a contact lens electrode were used The amplitude of the a and b-wave were measured compared and studied

RESULTS

1 Effect of serotonin The amplitude of the b wave decreased evidently half an hour after the administration of a relatively large dosage of serotonin (30 mg kg) and this effect continued for about 13 hours A series of subsequent studies with dosages of 20 10 and 5 mg per kg respectively indicated that a dosage of 20 mg or less caused no changes From these facts I suggest that there is a blood retinal barrier for this substance

(2) Effect of reserpine The evident decrease of the b wave could be observed within one hour after the administration of 2 mg per kg of reserpine, but its effect continued for about 24 hours

It is well known that reserpine has the effects of a general sedation and mild depression on the blood pressure Brodie and others found that following an intravenous administration of reserpine, the brain level of this substance reached its peak in half an hour and decreased rapidly thereafter, while that of serotonin fell to a low in about one hour where it continued for approximately 36 hours, after which a gradual recovery began This fact indicates that mild and long acting pharmacological effects of reserpine are caused by the serotonin it releases Assuming that the mechanisms in the brain are the same as those in the retina, it can be inferred from the above facts that the decrease of the b wave in the LRG is a secondary effect of serotonin in its free form, that is, released by reserpine

(3) Effect of JB-516 Then, we studied the effect of JB 516, a strong inhibitor of monoaminoxidase, which causes an abnormal accumulation of monoamines such as cathecolamines, serotonin and others in the tissue Slight elevation of both, the a- and b wave could be observed after the administration of 3 mg per kg of JB 516 This effect of JB 516 on the ERG continued for about 20 hours

Krill reported an experiment in which LSD 25 was applied as a hallucinogenetic substance rather than as an inhibitor of MAO He observed an enlarged b wave in the human electroretinogram and a disturbance of dark adaptation after LSD 25 was administered and he considered this increase of the b-wave as due to a functional disturbance of the retina caused by LSD 25 We considered that these electro retinographic changes, were the result of the retinal hyper excitation caused by amines, such as serotonin, which accumulated above the normal level under the effect of JB-516

(4) Effect of JB 516 and reserpine combined The changes of ERG were followed up after reserpine was administered to a rabbit pre medicated with JB 516 When 2 mg per kg of reserpine were ad ministered 24 hours after the administration of 3 mg per kg of JB 516, the decrease of the b wave was much more noticeable than after an application of reserpine alone This fact may imply that much of the serotonin was soon after released due to the influence of reserpine, as the noticeably decreased b wave reflected

(5) Effect of chlorpromazine For comparison with the effects caused by the substances used so far, we now applied chlorpromazine The administration of 3 mg per kg of chlorpromazine caused only a short, transient decrease of the b wave, not prolonged as serotonin produced it, which seems to be the effect of a different mechanism

(6) Effect of esidrex Esidrex, another blood pressure depressant, turned out to show hardly any effect on the electroretinogram

(7) Histochemical findings It was observed that the serotonin MAO existed in an normal rabbit retina and the activity of the serotonin MAO was changeable caused by the administration of serotonin (30 mg/kg) reserpine (3 mg/kg) and JB-516 (3 mg/kg)

SEROTONINE

ERB et Serotonine par Mme *Samson* — *DOLLFUS* (Discussion de la communication de M Juiduro Sugita)

Le hasard a fait que j ai enregistre, a titre de temoin une malade qui etait atteinte d une caranoidase avec depart de intestin grele, secretant la serotonine

J ai tojours hesite a placer ce sujet dans mes temoins, malgre tous des ophtalmologistes qui n avaient a me proposer aucun signe clinique au fond de l oeil En effet cet ERb ne me paraissait pas assez ample Je l avais enregistre peu apres l epreuve au porto qui favarisait la sécretion de serotonine

Retrospectivement, je me demande si cet ERb, dont l amplitude globale etait diminuee n etait pas du a la secretion de serotonine

SUMMARY

After studying the respective effects of intravenously administered serotonin reserpine and JB-516 on the ERG we consider that the release of serotonin in the retina decreases the b-wave while abnormal deposits of serotonin increase it The histochemical studies proved that *serotonin existed in an normal rabbit retina* Summing up we can say that serotonin plays an important role in the stimulus conduction mechanism of the retina

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METHODE

Nous nous sommes faith un devoir d etudier comment varient la grandeur et la forme de l ERG avec les differentes largeurs de la pupille L LRG etait enregistre a l aide d un electro encephalographe WTBG a 8 conduites Apres avoir provoque chez le malade une mydriase artificielle on adaptait le malade pendant 5 minutes a l il lumination de 25 Lx Pour l examen on avait choisi des individus ages de 18 à 30 ans Les stimulus lumineux de 5 000 Lx etaient pro duits par un eclair electronique d une duree d eclair lumineux de 0 002 secondes

PROCEDE DE TRAVAIL

1 Dans le premier groupe

Devant l oeil à examiner on placait a une distance de 15 mm du sommet de la cornee une plaquette avec une ouverture circulaire dont la grandeur etait changee de 0 5 mm à 3 0 mm par 0,5 mm Dans ce groupe nous avons enregistre au total dans 17 serie 236 ERG evaluables

2 Dans le deuxième groupe

Sur la lentille de contact nous avons place une pellicule ayant une ouverture circulaire dont nous avons change Il diametre en changeant les pellicules de 1 0 — 10 mm toujours par 1 mm Nous avons enré gistre dans 20 series 320 ERG evaluables et pour comparer les resultats nous avons choisi les malades du premier groupe

3 Dans le troisieme groupe

Comme stimulateur nous nous sommes servis au lieu de l eclair electronique des rayons lumineuses à une divergence de 5 et une grandeur lumineuse de 200 Lx Nous en avons illumine la region cen trale pendant un temps de stimulation de 0 01 sec L ouverture cir culaire dans la plaquette etait placee devant l oeil sous les memes conditions comme au premier groupe Nous avons enregistre en 18 series 352 ERG evaluables

4 Enfin

Nous nous sommes servis de lentilles de contacte qui a l exception de l ouverture circulaire au centre ayant un diametre de 2 mm etaient fabriquees d un materiel tout à fait opaque Ce groupe devait verifier dans quelle mesure le facteur de la lumière dispersee penetrant du coté et le facteur de la lumière passant par le sclère pourraient de former l ERG Nous avons enregistrex en 15 series 130 ERG evalu ables

RESULTATS

Dans les valeurs moyennes du premier groupe examine on pouvait observer que l onde a et b accroit avec la grandeur de la surface de l ouverture de la plaquette preposee En plus on pouvait remarquer une diminution de la somme du temps de latence du temps de duree de la composante positive de l onde b Il nous intéressait surtout si

L'INFLUENCE DE LA PUPILLE ARTIFICIELLE SUR LA GRANDEUR ET LA FORME DE L'ELECTRORETINOGRAMME

JAN VANYSEK, VLADIMÍR KOZOUSEK

De la clinique ophthalmologique de la Faculté de la Médecine de l'Université J. E. Purkyně à Brno, Directeur Professeur MUDr Jan Vanysek, Dr Sc

Le problème de stimulus lumineux joue un rôle important dans des grands efforts que l'on fait pour standardiser les méthodes électrorétinographiques. L'étendue de l'illumination de la rétine sert de mesure de l'irritation des fotorécepteurs réagissant à la lumière. Cette illumination de la rétine /I/ dépend de toute une série de facteurs. Ce sont la clarté de la source lumineuse /B/, la pénétrabilité du milieu /d/, la surface de la pupille /Fp/, la distance objective focale de la source lumineuse /f/. D'après Schober /1/ la dépendence suivante est valide:

$$I = \frac{d\ B\ Fp}{f^2}$$

Aujourd'hui nous allons nous occuper du facteur de la surface de la pupille qui est important pour l'étendue de l'illumination de la rétine. L'étendue de la surface de la pupille a de plus aussi une grande influence sur le cours de l'adaptation. La largeur de la rétine est donnée par les faits régulationes nerfeuses, les influences psychiques, l'état maladif, l'âge etc. Hattinger /2/ a étudié la question de l'influence de l'âge sur la largeur de la pupille. Mise à part la période de l'enfance et de la sénilité, la largeur se trouve d'après Schober dans une dépendence linéaire au logarithme de illumination. La largeur de la pupille varie entre 1,5 et 8 mm. C'est à dire que la surface de la pupille varie entre 1,7 et 50 mm². La surface de la pupille a donc une grande influence sur l'étendue de l'illumination de la rétine. On sait que l'étendue de l'illumination de la rétine détermine la grandeur et la forme de l'ERG. De cette question s'occupaient déjà tout un nombre d'auteurs comme Asher /4/, Boyenton /5/, Greed, Granit /6/, Frey, Bartley /7/, Granit /8/, Granit, Rubinstein, Thorman /9/, Kupe /10/, Kuffler /11/, Riggs, Berry, Wayner /12/, Wirth, Zetterstrom /13/ et autres. Les résultats donnés par les divers auteurs ne sont pas identiques. Nous voulions vérifier les résultats de nos études précédentes non publiées de l'année 1958 que l'onde b augmente linéalement avec l'augmentation logarithmique de la surface de la pupille artificielle ce qui correspond à la loi généralement valide de Weber-Fechner qui dit que la perception augmente linéalement avec le logarithme de l'excitation.

METHODE

Nous nous sommes fait un devoir d etudier comment varient la grandeur et la forme de l ERG avec les differentes largeurs de la pupille L ERG etait enregistre a l aide d un electro encephalographe WTBG a 8 conduites Apres avoir provoque chez le malade une mydriase artificielle on adaptait le malade pendant 5 minutes a l il lumination de 25 Lx Pour l examen on avait choisi des indiv dus ages de 18 a 30 ans Les stimulus lumineux de 5 000 Lx etaient pro duits par un eclair electronique d une duree d eclair lumineux de 0 002 secondes

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2 Dans le deuxieme groupe

Sur la lentille de contact nous avons place une pellicule ayant une ouverture circulaire dont nous avons change il diametre en changeant les pellicules de 1 0 — 4 0 mm toujours par 1 mm Nous avons enre gistré dans 20 series 320 ERG evaluables et pour comparer les resultats nous avons choisi les malades du premier groupe

3 Dans le troisieme groupe

Comme stimulateur nous nous sommes servis au lieu de l'éclair electronique des rayons lumineuses a une divergence de 5 et une grandeur lumineuse de 200 Lx Nous en avons illuminé la region cen trale pendant un temps de stimulation de 0 01 sec L ouverture cir culaire dans la plaquette etait placee devant l oeil sous les memes conditions comme au premier groupe Nous avons enregistre en 18 series 352 ERG evaluables

4 Enfin

Nous nous sommes servis de lentilles de contacte qui a l exception de l ouverture circulaire au centre ayant un diametre de 2 mm etaient fabriquées d un materiel tout a fait opaque Ce groupe devait verifier dans quelle mesure le facteur de la lumière dispersée penetrant du coté et le facteur de la lumiere passant par le sclere pourraient de former l ERG Nous avons enregistrex en 13 series 130 ERG evalu ables

RESULTATS

Dans les valeurs moyennes du premier groupe examiné on pouvait observer que l onde a et b accroit avec la grandeur de la surface de l ouverture de la plaquette preposee En plus on pouvait remarquer une diminution de la somme du temps de latence du temps de duree de la composante positive de l onde b Il nous interessait surtout si

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Le probleme de stimulus lumineux joue un role important dans des grands efforts que l on fait pour standardiser les methodes electroretinographiques L'etendue de l illumination de la retine sert de mesure de l irritation des fotorecepteurs reagissant a la lumiere Cette illumination de la retine /E/ depend de toute une serie de facteurs Ce sont la clarete de la source lumineuse /B/, la penetrabilite du milieu d , la surface de la pupille /Fp/, la distance objective focale de la source lumineuse f D'apres Schober /1 la dependence suivante est valide

$$L = \frac{d\ B\ Fp}{f^2}$$

Aujourd hui nous allons nous occuper du facteur de la surface de la pupille qui est important pour l etendue de l illumination de la retine L etendue de la surface de la pupille a de plus aussi une grande influence sur le cours de l adaptation La largeur de la retine est donnee par les faits regulatoires nerfeuses les influences psychiques, l etat maladif l age, etc Hartinger 2 a etudie la question de l influence de l age sur la largeur de la pupille Mise a part la periode de l enfance et de la senilite, la largeur se trouve d apres Schober dans une dependence lineaire au logarithme de illumination La largeur de la pupille varie entre 1 5 et 8 mm C est a dire que la surface de *la pupille varie entre 1 7 et 50 mm La surface de la pupille* a donc une grande influence sur l etendue de l illumination de la retine On sait que l etendue de l illumination de la retine determine la grandeur et la forme de l'ERG De cette question s occupaient deja tout un nombre d auteurs comme Asher /4/, Boventon 5 Greed, Granit 6 Frey, Bartley /7/, Granit /8/, Granit Rubinstein Thorman 9 Knave /10/, Kuffler /11/, Riggs, Berry, Wayner 12, Wirth, Zetterstrom /13/ et autres Les resultats donnes par les divers auteurs ne sont pas identiques Nous voulions verifier les resultats de nos etudes precedentes non publiees de l annee 1958 que l onde b augmente lineairement avec l augmentation logarithmique de la surface de la pupille artificielle ce qui correspond a la loi generalement valide de Weber Fechner qui dit que la perception augmente lineairement avec le logarithme de l'excitation

The fibrous strands arising from the retina, and which ultimately lead to its detachment, are particularly characteristic, appearing tubular in section with a fibrous core and a cellular covering (Fig 9), they extend in a serpentine fashion from the inner substance of the



Fig 8 Eales's disease Flat section of retina showing hyaline thickening of a small vein and perivascular pigmentation Haematoxylin and eosin × 280

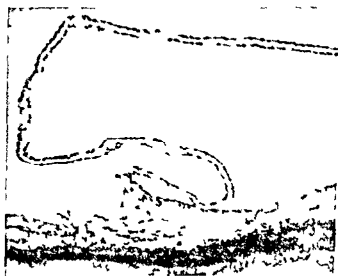


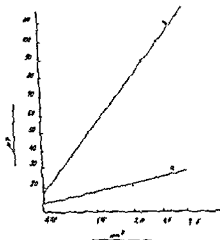
Fig 9 Eales's disease Fibrous strand in the vitreous arising from the retinal surface Haematoxylin and eosin × 112

stratum opticum and course along the face of the vitreous in areas where it is detached In fact the vitreous detachment appears to be intimately concerned in their formation

From my own pathological examinations it would seem that uveitis is not an essential accompaniment In one typical case, in a

et sur l axe y le potentiel de l onde a et de l onde b Le graph indique que meme ici il n y a pas de dependence logarithmique

3 Dans le troisieme groupe ou nous avons employe un stimulus de 200 Lx avec une exposition prolongee de 0,002 a 0 01 secondes nous avons porte la moyenne des resultats sur le graph 3 qui montre une augmentation linéaire de l onde a et de l onde b avec une augmentation logarithmique de la surface de l ouverture artificielle

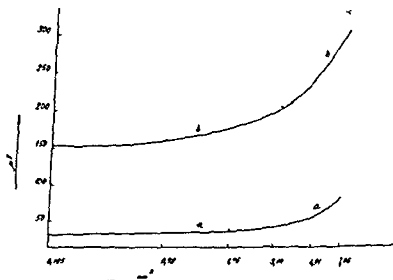


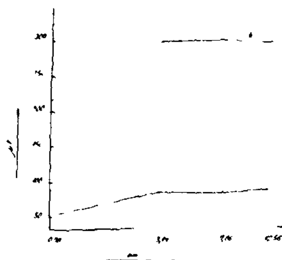
4 Dans le quatrième groupe examiné a l aide d une lentille de contacte en materiel opaque et une ouverture au milieu d un diamètre de 2 mm nous avons pu comparer les resultats obtenus a l aide d une ouverture de la meme grandeur les valeurs moyennes du potentiel de l onde b etaient plus petites que celles obtenues avec les ouvertures au meme diamètre dans les autres groupes et un signe frappant de ce groupe était qu en se servant del eclair électronique les series des l'ERG étaient par la forme du developpement de l ERG egales en comparaison avec les examens en serie des groupes precedents

DISCUSSION

Pour le moment il est difficile de dire quelle est la largeur la plus avantageuse de la lentille artificielle Par rapport a lintensite lumineuse de l eclair électronique nous pensons que l ouverture la plus avantageuse était l ouverture circulaire jusqu a 2 mm de diametre L elimination de l influence de la lumière dispersee est un autre element interessant provenant d un parcours different des courbes obtenues par la preposition de la plaquette en utilisant un éclair eletronique et des rayons presque parallèles du stimulus lumineux La meilleure loi presumée et exprimée de l augmentation de l onde a et de l onde b d apres la loi de Weber Fechner semble dependre dans les rayons presque parallèles du stimulus lumineux surtout de l elimination de la lumière dispersée

quelques unes de ces courbes s'approchent du parcours logarithmique et c'est pourquoi nous avons designe les resultats moyens dans certains exemples dans le tableau 1 et dans le graph 1 ou sur l axe x est portee la surface de l ouverture *dans une echelle logarithmique et sur l axe* y le potentiel de l'onde a et de l onde b Dans la largeur physiologique de la pupille on peut observer avec la surface augmentante de l ouverture une augmentation de l'onde a et de l onde b En comparant le parcours *entier il ne s'agit pas d'une* dependence logarithmique continuelle





2 La moyenne des resultats obtenus au deuxieme groupe avec les pellicules est donnee dans quelques exemples au tableau 2 et au *graph* 2, ou sur l'axe x est portee la surface dans l echelle *logarithmique*

Malad	D met de l'ouvertu e ci cula e dans la plaqu tte																	
	3 0 mm			5 mm			2 0 mm			1 5 mm			1 0 mm			0 5 mm		
	My ne d paten c l e m o l		My une n e l mes de s c															
	a	b	t	a	b	t	a	b	t	a	b	t	a	b	t	a	b	t
1	C4 0	241 0	6 6	30 0	190 0	2[illegible]	50 0	193 0	7 3	29 8	155 0	7 6	28 2	133 0	7 4	23 3	148 0	8 3
2	53 5	229 0	7 8	43 1	1 6 0	8 3	34 1	145 0	8 1	33 4	147 0	8 8	32 2	126 0	9 1	34 8	114 0	8 8
3	95 5	314 0	5 5	77 4	286 0	6 1	67 5	[illegible]	6 6	55 0	260 0	7 1	56 3	247 0	7 6	45 0	219 0	7 6
7	33 2	234 0	6 4	4[illegible] 5	202 0	7 1	35 3	183 0	7 1	48 0	204 0	7 6	35 6	168 0	7 4	25 4	13[illegible] 0	7 2
Moyenne totale	88 5	334 3	—	48 7	212 0	—	48 9	211 5	—	40 7	198 6	—	37 6	166 4	—	32 0	154 4	—
Nombre des mésurages	26	2[illegible]	26	33	33	33	37	37	37	33	33	33	33	33	33	33	33	33

Malade	Oeil	Diametre de l'ouverture circulaire dans la pellicule											
		4 0 mm			3 0 mm			2 0 mm			1 0 mm		
		Diametre du potential en micro V		moyenne en centiemes de sec									
		a	b	t	a	b	t	a	b	t	a	b	t
1	OD	68 2	256 0	—	47 4	232 0	—	—	—	—	39 8	205 0	—
	OS	91 0	278 0	—	59 5	256 4	—	—	—	—	45 2	230 8	—
	Moyenne OD + OS	74 6	267 0	—	53 4	244,2	—	—	—	—	42 5	217 9	—
2	OD	70 5	266 0	7 6	109 5	354 0	7 0	100 0	340 0	7 1	38 5	176 5	11 3
	OS	80 0	295 0	6 9	91 5	384 0	7 0	93 5	386 0	7 0	39 8	163 5	8 4
	Moyenne OD + OS	75 2	280 5	7 2	100 5	369 0	7 0	96 7	363 0	7 0	39 1	165 0	9 8
4	OD	74 5	246 0	4 8	115 0	344 0	5 2	123 8	238 0	7 3	18 7	234 0	7 1
	OS	163 0	455 0	4 9	146 0	494 0	5 3	141 0	482 0	7 1	96 0	407 0	6 9
	Moyenne OD + OS	118 7	350 5	4 8	130 5	419 0	5 2	132 4	390 0	7 2	72 3	319 2	7 0
5	OD	83 3	230 0	6 4	87 2	254 0	7 9	86 0	244 0	8 0	56 8	204 0	7 0
	OS	101 0	368 0	5 5	85 2	317 0	7 8	81 6	306 0	7 0	73 0	232 0	7 1
	Moyenne OD + OS	92 1	299 0	5 9	86 2	285 5	7 8	83 8	267 8	7 5	68 2	262 6	7 7
7	OD	66 0	270 0	6 9	36 8	137 0	6 4	33 0	201 0	6 6	21 4	100 0	6 3
	OS	111 0	290 0	6,5	57 2	266 0	6 6	36 6	157 0	6 8	23 4	157 0	6 9
	Moyenne OD + OS	85 2	278 5	6 9	47 3	223 4	6 5	34 8	159 0	6 7	22 4	166 6	6 3
Moyenne totale		88 4	295 2	—	87 2	305 3	—	85 2	301 8	—	50 8	216 9	—
Nombre des mésurages		65	65	53	75	75	63	54	54	54	77	77	65

DISCUSSION

ELECTRO DIAGNOSTIC TEST BASED ON THE STANDING POTENTIAL OF THE EYE

ARDEN, G B (*U K*)

Electrodes placed on the skin over the eyes record potentials associated with eye movements which can be used to estimate the magnitude of the intra ocular potential generators These vary in size as retinal illumination is altered with a time course demonstrating that the potentional is related to the metabolism of the outer retina The clinical test (the EOG) based on these findings can be used in the diagnosis of many types of retinal le ion and is especially sensitive in the detection of degenerations and abnormalities in blood supply

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EXPERIMENTAL STUDIES ON THE EYE MOVEMENT BY MEANS OF SIMULTANEOUS RECORDING PHOTO ELECTRONYSTAGMOGRAM

HATAKEYAMA AKINI (*Japan*)

A new arrangement of the photoelectronystagmogram (PNG) has been designed as follows The image of the subject eye is focused by a telelens on the narrow slit set up in front of a photomultiplier tube The image of the iris and the sclera is allowed to situate on the narrow slit after simple adjustment through a window which is opened on the upper corner of the opt cal box In order to carry out our experiments two optical systems of the same s ructure were prepared

Firstly PNG of horizontal components of right and left eye has been recorded simultaneously Secondly we have recorded the diagonal component at angles of 45 and 135 degrees on one eye and thirdly we recorded eye movement with one system and the face movement with the other

From these experimental results the relationships between opto kinetic nystagmus fixation reflex and fusional movement of each eye have been discussed

La constance relative des courbes de l'ERG en employant des lentilles opaques avec une pupille artificielle de 2mm semble etre une recommandation pour l'emploi de cette lentille pour l'oeil cycloplegique pour la standardisation de la méthode

CONCLUSION

Les quatre groupes des resultats presentes semblent indiquer que les recherches sur l'influence de la pupille sur l'ERG devraient etudier

1 l'intensite la plus favorable de stimulus lumineux du point de vue de la loi Weber-Fechner

2 Assurer a la pupille artificielle dans la lentille de contacte la quantité standard de lumière entrant l'oeil

3 Eliminer l'effet de la lumiere dispersee et de la lumiere passant ainsi aussi par le sclere

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however, an electro oculogram (EOG) could not be recorded before the subject was able to cooperate voluntarily, producing eyemovements necessary for the measurement of the standing potential

The present paper describes, among other things a technique which has been developed for the recording of the EOG in children in narcosis The procedure described is applicable and has been applied already shortly after birth

The results of such a combined electro diagnostic procedure in children suspected of developing tapeto retinal degeneration of various origin are discussed

PROCEDURE

In the standard recording of the ERG, both single flash and flickering light stimuli have been applied The single flash technique (using a blue filter (Gevaert B 488)) is particularly meant for the recording of scotopic activity The flicker ERG using the technique of selective amplification of the flickering response (Henkes, van der Tweel and Denier van der Gon (3)) is recorded in order to be able to construct an I/CFF curve (intensity versus flicker fusion frequency) for the photopic mechanism using arbitrarily the following frequencies 20 30 40 60 and eventually 70 flashes per second Stimulus source electronic stroboscope (van Gogh) with frequency independent intensity steps of relative intensity 1 2 4 8 Reduction in intensity is done with the help of neutral density filters of a factor 8 and 64 Recording apparatus 6 channel van Gogh EEG machine with 1-channel frequency analyser The time constant used for the recording of the single flash ERG is 1 second for the recording of the flicker ERG 0 03 sec — Normal range of maximum scotopic b wave (measured from the trough of the a wave — if present —) varies between 250 and 530 microvolts Values lower than 210 microvolts are considered probably subnormal and lower than 180 microvolts to be *definitely subnormal*

Normal limits of I/CFF curve is given in the figures Aberration from the normal course is judged referring to the standard curve

The standard recording of the EOG — giving information concerning the standing potential of the eye — asks for excursions of the eye over a given angle — in our setup 30 degrees — in the horizontal plane which produces a potential difference between electrodes mounted on the temporal and the nasal margin of the orbit (figure 1 a) The potential produced varies among other things with the adaptive state of the retina (figure 1 b) The EOG potential partly derives from the cornea This part is of the opposite sign and reduces the final potential recorded

Our standard technique of EOG recording is essentially the same as used by Arden recording *of the EOG* in dark adaptation up to 12 minutes Light adaptation (adapting level 20 000 Trolands) and continuation of recordings every *minute* to approx 30 minutes Reduction or loss of EOG refers primarily to the change in voltage

THE ROLE OF ELECTRORETINOGRAPHY AND ELECTRO OCULOGRAPHY IN THE EARLY DIAGNOSIS OF TAPETO RETINAL DEGENERATION IN CHILDREN

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INTRODUCTION

In the early diagnosis of retinal disorders of degenerative origin the application of combined diagnostic techniques seems to be essential. Apart from the indisputable value of electroretinography as a diagnostic tool of primordial value electro oculography comes more and more to the fore (see Arden's paper of this meeting).

Nowadays we know that photoreceptors, bipolar cells and the intra retinal cell systems belonging to the two retinal mechanisms, all contribute to the development of the ERG.

On the other hand, the condition of choroid, Bruch's membrane, pigment epithelium and outerlimbs of the photoreceptors is reflected in the standing potential of the eye. The recording of this potential seems thus crucial for the objective judgement of the functional ability of these structures.

It is clear that both recordings, of ERG and EOG, are necessary in order to get the maximum information regarding the function of retina and choroid.

According to Arden and co-workers (1a b), the initial stages of degenerative retinal affections can be diagnosed more readily while using an electro oculographic examination. The alterations demonstrable in the EOG recording are said to precede those found in the ERG.

Karpe (2) reported already a number of years ago that an extinguished ERG had been found in an ophthalmoscopically normal child of 7 months, of a mother suffering from a dominant tapeto retinal dystrophy. In most cases, however, the affection is said to develop at a later stage.

All in all, electro diagnostic procedures seem to be essential in the examination of those children, who are prone to get a degenerative retinal affection even before fundal changes have appeared. The latter are, as we know, relatively late signs of irreparable alterations of retinal function.

From the above, it is clear that the earlier these diagnostic procedures may be applied, the better. An electroretinographic examination can be performed—as we all know—almost from birth on. Thusfar,

(1) This report was produced in cooperation with the Netherlands General Association for Prevention of Blindness.

For the recording of the EOG in the young patient a special technique has been developed (Henkes and Verduin (4)) which copes with the difficulties encountered by the recording in children unable — due to their age — to carry out instructions The recording is done in narcosis which enables us to carry out the recording even in infants Besides the narcosis eliminates the troublesome nystagmus if present Recording is done — as in the standard technique — in dark and light adaptation

Use is made of low vacuum contact lenses of Worst (5) developed for the localisation of intra ocular foreign bodies The eyes are mounted with contact lenses provided with an extra long shaft The shafts of both lenses are fixed in a kind of ruler which is allowed to move in a kind of trial frame over a given distance producing an excursion of the eyes over a given angle of vision (see figures 2 a and b 3) The eyes are forced to move due to the suction system Simple movement of the ruler is sufficient to produce the desired EOG (*)

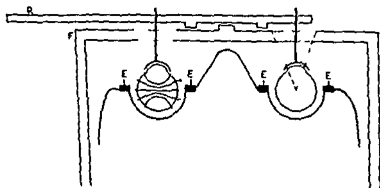


Fig A Schematic drawing of EOG technique applicable in narcosis The eyes mounted with low vacuums contactlenses provided with a metal shaft are forced to follow movement of ruler (R) while shifted over a given angle

The EOG produced is essential the same as found under standard conditions
E electrodes F trial frame

Naturally an exact comparison between the results obtained with the standard technique and this special technique devised for the recording of the EOG in narcosis, is impossible (influence of narcosis on the EOG differences in age difference in angle over which the eyes are moved etc)

(*) The frame and contactlenses etc have been designed and produced by Medical Workshop Herrsingel 28 Groningen Netherlands

under the influence of changing conditions of light and dark adaptation The voltage of the EOG itself is reduced as well. The normal variation in the basic voltage, however, differs even between normal eyes substantially due e g , to the amount of proptosis

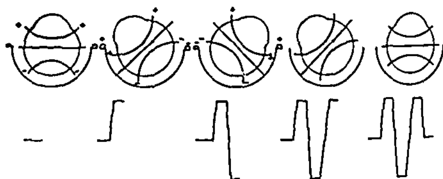
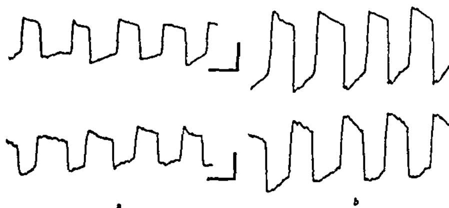


Fig 1 A Recording of standing potential based upon alterations in the electric field of the eye following eye movements in the plane of the electrodes



B The upper tracing of the original graphs records movements of the right eyes the lower of the left eye The trace begins with a movement of the eyes to the left after which the subjects look rhythmically from one fixation light to another In between the eye movements the pens return towards the base line owing to the time constant of the amplifiers The amplitude of the vertical excursions is a measure of the magnitude of the standing potential (a) after 12 min dark adaptation (b) 8 min after re-illuminating the retina Calibration bars 500 micro Volts/500 msec (after Arden and Kelly J Physiol 161 189 204 (1962))

According to Arden and co workers the mean increase in voltage following intensive light adaptation is 252% An increase of 200% is suspected and an increase less than 185% is considered as definitely abnormal

viral in which immune mechanisms are especially prominent and in which hypersensitivity is known to develop

ASSOCIATION WITH NERVOUS MANIFESTATIONS

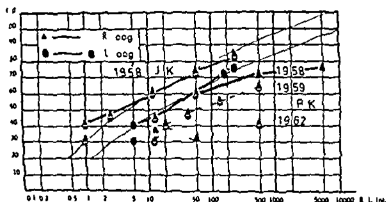
There seems to be no doubt that retinal perivasculitis can occur in association with nervous manifestations — an incidence of 16 per cent has been quoted (Ballantyne and Michaelson, 1948) The suggestion has been made that this is due to a coincidental periphlebitis of the cerebral vessels (Axenfeld 1921, 1927, 1930) and some of the conditions reported are apoplexy (von Graefe, 1854) convulsions (Ballantyne 1909), transient paralysis (Lowenstein, 1931) polyneuritis (Duvoir and Bernard 1933) epilepsy (Haverkorn van Rijsewijk, 1938) paraplegia (Silfverskiold 1947) and severe headaches (Veirs, 1948), but most notably it has been described in association with multiple sclerosis (Ter Braak and van Herwaarden 1933 Rucker, 1945, 1947, Haar, 1948 1949 1953 Wybar 1952 Gougard and Paris 1954 Hagedoorn 1955 Orban 1955 Paufique and Etienne 1955 Shubova and Konchakova 1957) in which disease retinal periphlebitis has a reported incidence varying from 10 to 40 per cent (Donders 1958)

It is questionable however, whether many of these cases should be considered in the category of Eales s disease since predominance in the male sex was not always a feature and retinal haemorrhages and retinitis proliferans were frequently absent Moreover as suggested by Jefferson and Cloake (1952) there is the possibility that the retinal and neurological manifestations may co exist by chance It is of interest that recent clinical investigations have obtained contradictory evidence Thus Silfverskiold (1947) reported 22 and Jefferson and Cloake (1952) six typical cases of Eales s disease showing no evidence of neurological involvement whereas White (1961) found neurological disorders in seven of 17 typical cases Conversely Donders (1958) found no evidence of retinal vasculitis in 25 cases of multiple sclerosis whereas Scott (1961) found sheathing of the retinal veins in seven of 65 cases

The most recent view is that of White (1961) who maintains that the association is a real one and that the retinal vasculitis is a non-specific inflammatory lesion which probably occurs in the vessels of the parenchyma and meningeal coverings of the brain and spinal cord According to him the fact that similar lesions may develop in the central retinal vein as originally shown by Ballantyne and Michaelson 1937 and by Verhoeff and Simpson (1940) and more recently by Ible and Wybar (1961) merely emphasises the anatomical and functional continuity between the retina and the remainder of the central nervous system

Are we to assume then that Eales s disease is the retinal expression of a vasculitis which may affect the whole central nervous system? This is a crucial question which cannot yet be decided for it appears as often denied as supported Francois and Neetens (1959) in describing a characteristic instance of sheathing of the retinal veins in a case of

media and fundi normal In the ERG, the maximum scotopic b wave recorded was 250 microvolts in both eyes *The I/CFF curve* gave a *normal* course for the photopic retinal mechanism (figure 4 a) The conclusion reached at that moment was that the boy was not prone to get the disease Up to the present at the age of 8, the boy is completely normal



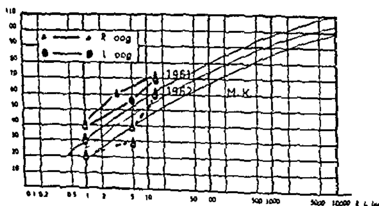
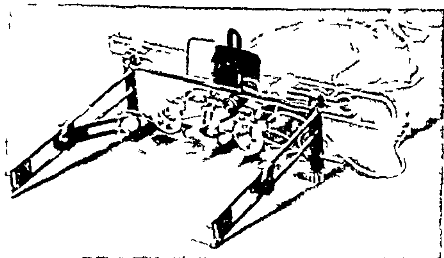


Fig 4 I/CFF curves (photopic branch) of 3 brothers belonging to a family in which cerebromacular degeneration *occurs. J K shows* a normal curve. This child now (1962) 9 years of age developed normally P K and M K are affected The course of the I/CFF curves *in* both children points clearly towards a deterioration of the process. These *findings* are corroborated by the EOG-data

(*b*) His elder brother Peter K was examined at the age of 6 on the same date as the first examination of Johannes K. There were



B The trial frame ready for mounting



Fig 3 Child in narcosis mounted with contactlenses and trial frame and prepared for EOG examination

RESULTS

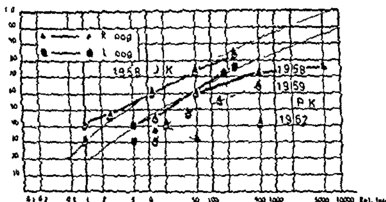
The value of a combined ERG and EOG examination is demonstrated by the following case reports derived from two families suffering respectively from a cerebro macular degeneration type Spielmeyer – Vogt — Batten — Mayou, and from a tapeto retinal degeneration of intermediate X chromosomal inheritance

Cerebro macular degeneration, juvenile amaurotic idiocy

We had the opportunity to examine at an early age three siblings of a family in which the above mentioned disease is known to occur

(*a*) Johannes K was examined for the first time in 1958 at the age of 5 He had no complaints whatever Visual acuity 1 0 Optic

media and fundi normal In the ERG the maximum scotopic b wave recorded was 250 microvolts in both eyes The I/CFF curve gave a normal course for the photopic retinal mechanism (figure 4 a) The conclusion reached at that moment was that the boy was not prone to get the disease Up to the present at the age of 8, the boy is completely normal



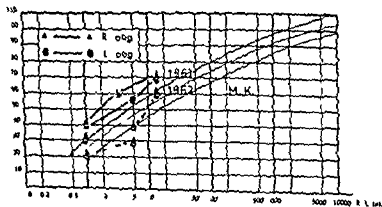
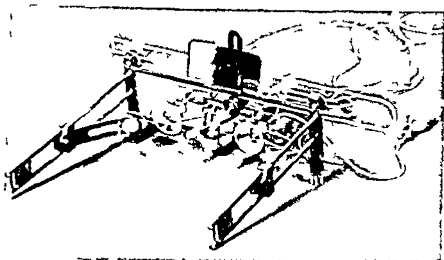


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(a) Pieter J was examined at the age of 2, in *1961* Optic *media* and fundi normal Single flash ERG and flicker ERG normal scotopic and photopic responses Th s boy was suspected for having the disease, as a brother was definitely affected The mother is a carrier of the disease although her fundus oculi does not show the abnormality of a tapetum lucidum like picture described by Falls and Cotterman (6) One year later the fundus had changed in the peri phery of the fundus a very slight pigmentary alteration *seemed to* have appeared The single flash ERG now revealed a sub-normal *scotopic* activity (on the right eye a maximum scotopic response of 140 microvolts on the left eye not recordable due to technical difficulties) The photopic I/CFF curve revealed a probable normal photopic activity *though due to* the technical difficulties encountered the precise interpretation was impossible The EOG however, supported the ERG finding in as far as *the increase* in potential following light adaptation was definitely subnormal It is most probable that this boy will be clearly affected within a relatively short period

(*b*) Johannes B a healthy boy of 2 years of age, had no alterations whatever His grandfather of mother s side is known to suffer from the disease His mother and Pieter J s mother are sisters His mother does not show any abnormalities in the optic media and the fundi oculi The ERG of the boy was completely normal regarding the single flash — and the flicker ERG responses

At the renewed examination one year later neither media nor fundi showed abnormalities The ERG and the EOG however *showed definitely alterations which point towards* the existence of the disease the scotopic response is subnormal the increase in light adaptation in the EOG is lacking (see figure 5) It is clear that this boy *at the* age of 3 shows already the affection clearly in the electrophysiological results

(*c*) A B a sister of J B was 1½ years of age at the time *of examination* The fundi presented no abnormalities However both scotopic ERG— and EOG-data pointed towards a *definite* disturbance in retinal activity The maximum scotopic b-potential *recorded* was 85 and 75 microvolts for right and left eye *respectively The* EOG-curve (figure 5) lacked the normal rise after light adaptation *It closely resembled* in its course the ones known from the beginning stages of tapeto retinal degeneration *In this family* more heterozygotic female-carriers are known who *suffer* from severe deterioration of retinal function *For the first time however we were able to* diagnose the affection already in a young girl

DISCUSSION

From the above it appears that application of electro diagnostic procedures is essential in *order to ensure* the diagnosis at the earliest possible moment

no visual complaints His parents, however, feared that he might be affected as they observed a change in his behaviour, just like they had observed in two elder children (a brother and sister of this boy), who became affected — Visual acuity 1 0 Optic media no abnormalities Funduscopy doubtful temporal pallor of the discs Macular region slight alterations No pigmentary degeneration visible The ERG showed markedly reduced scotopic responses, the maximum scotopic b potentials being 55 and 70 microvolts Photopic activity, judged upon the course of the I/CFF curve, showed only a slightly aberrant course (see figure 4 a) Diagnosis was made at this moment on the existence of the cerebro macular degeneration, though still in its initial stage One year later, his visual acuity was still normal Funduscopy however, revealed some more atrophy of the optic discs and a possible increase in the slight macular alterations described one year before Scotopic activity, judged upon the single flash ERG, was completely extinguished Photopic activity, expressed in the I/CFF curve, was slightly reduced Three years later, at the age of 10, visual acuity had been markedly deteriorated fingers counting at 1 meter in both eyes The fundi revealed pronounced alterations white discs, narrow vessels, abundant pigmentary degeneration both in the central area and in the periphery The ERG was now completely extinguished, except for a rudimentary photopic response, demonstrating only following selective amplification of the flickering response (see figure 4 a) The EOG was of very low voltage too At the same time any increase in voltage following light adaptation was missing (figure 5)

(*c*) The younger brother, Marinus K , was first examined in 1961, at the age of 2 Neither in the optic media, nor in the fundus abnormalities were found The ERG was normal maximum b potentials of right and left eye respectively were 255 and 220 microvolts The course of the I/CFF curve was normal (figure 4 b) Based upon the results available, the prognosis for this child was considered relatively good However, one year and a half later, at the age of 3, the parents came to us for a renewed examination, as the child seemed to have changed his behaviour Though fundouscopy did not reveal the slightest alterations, the scotopic ERG pointed towards an important loss of retinal activity Only a rudimentary scotopic response could be demonstrated Photopic activity however was still almost normal (see figure 4 b) The EOG too, was seriously affected No significant increase followed the intense light adaptation (see figure 5) It is clear that this boy of only 3 years is already definitely affected The result of both ERG and EOG examination point towards the same bad prognosis

Intermediate X chromosomal tapeto retinal degeneration

In a family in which the above mentioned disease is known to occur, the below mentioned siblings have been examined in which a combined electro diagnostic examination seemed to be of importance

LITERATURE

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(3) Henkes H E Van Der Tweel L H and Denier Van Der Gon J J 1956 Selective amplification of the electroretinogram *Ophthalmologica* 132 140–150
(4) Henkes H E and Verduin P C. Dysgenesis or abiotrophy? — Thoughts about Leber's congenital amaurosis *Ophthalmologica* 145, 144–160 (1963)
(5) Worst J and Otter K. 1961 Low vacuum diagnostic contact lenses *Am J Ophthalm* 51 410–424
(6) Falls H F and Cotterman C W 1948 *Choriodoretinal degeneration Arch Ophth* 40 685–703

PERIODICAL VIBRATIONS ON THE ELECTROMYOGRAM OF THE EXTRAOCULAR MUSCLES

KUBOKI TETSUYA and DOMON EMI (*Japan*)

Since 1953 electromyography of the extraocular muscles has been one of the studies in ophthalmology However, basic information about these particular muscles has been lacking We will report here on some basic features of the electromyograph of these muscles, especially the internal rectus

Fig 1 As an electrode a single needle electrode made of a steel wire with a diameter of 0 3 mm was applied It was insulated with paint made of synthetic resin except for the tip The needle *usually* was inserted into the muscle through the skin of the orbital margin This slide shows the needle having been inserted to examine the internal rectus

Fig 2 This figure represents three patterns of the electromyograph of an extraocular muscle The top recording shows single oscillations of a single motor unit It is obtained with a needle electrode having a very small naked area at the tip The middle recording shows an interference pattern which is recorded with a needle having a relatively large naked area at the tip The bottom recording was obtained by our own original method This periodical wave is the result of summation of single oscillations of many motor units The chief components of our method are firstly relatively large naked area on the needle secondly, some distance between the muscle and the needle and thirdly high velocity of recording

This is not only true for the types of tapeto retinal degeneration mentioned above but also for any other type of degeneration e g, the amaurosis congenita Leber (Henkes and Verduin (4))

Apart from this, a combined electrodiagnostic procedure as described above, may reveal the fact that—though funduscopy seems to restrict the degenerative process to a certain area, e g, the macular

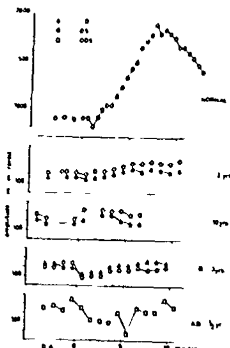


FIG. 5 EOG-curve recorded in a normal subject compared with EOG-curves recorded in narcosis. Setup described in text. Curves recorded in children P K and M K (cerebromacular degeneration) and J B and A B (X chromosomal tapetoretinal degeneration) are definitely abnormal and identical with EOG-curves found in fully developed tapeto-retinal degeneration

region — the whole of the retinal system actually is affected Such conditions have been encountered repeatedly in the juvenile macular degeneration The implication of such, however, will be discussed elsewhere

CONCLUSIONS

1 Electro diagnostic procedures (ERG and EOG) are essential in order to ensure the diagnosis in degenerative disorders of the retina at the earliest moment possible,

2 Recording of scotopic ERG and of EOG is the procedure demonstrating at the earliest moment of alterations, even before the fundi oculi show alterations whatever The photopic flicker ERG (photopic branch of CFF curve) gives the deteriorations only at a later stage,

3 An EOG examination in narcosis is a simple procedure Its introduction in the routine procedure of electro diagnosis of retinal disorders is worth while

SUMMARY

A combined electro diagnostic procedure consisting of electro-retinography and electro-oculography is advocated in the diagnosis of tapeto-retinal degenerations in the young child

LITERATURE

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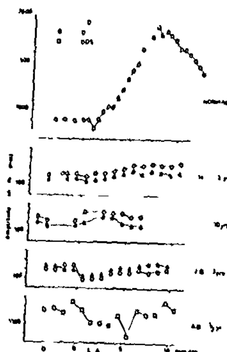


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SUMMARY

A combined electro-diagnostic procedure consisting of electro-retinography and electro oculography is advocated in the diagnosis of tapeto-retinal degenerations in the young child

although, as I have already pointed out, the classical picture of Eales's disease was not reproduced. Elliot (1954, 1958) is perhaps the most enthusiastic protagonist of the tuberculous allergy theory today, and from his extensive personal experience of a large series of 55 cases would attribute all cases to this cause. He cites focal reactions in the retina after the injection of tuberculin as an indication of this aetiology, a point previously made by Werdenberg (1940) and Lang (1955). White (1961) found a high degree of cutaneous sensitivity to old tuberculin in 10 of 15 cases of retinal vasculitis.

There are two further associations which strengthen this view. First, Eales's disease has been reported in association with *sarcoidosis*, both with and without uveitis, and whatever the aetiology of sarcoidosis it surely — at least in some instances — bears a relation to tuberculosis. It is known that the sarcoid granulomatous reactions may selectively affect the retinal vessels (Gould and Kaufman, 1961; Witmer, 1948), although not producing the fundus picture of Eales's disease. Secondly, the histology of retinal vasculitis is similar to that of *erythema nodosum* (Haar, 1948) which also had a high incidence of tuberculosis, and also in sarcoidosis (Vesey and Wilkinson, 1959). It could be postulated therefore that Eales's disease is a vasculitis of the same nature as erythema nodosum, the one affecting the retinal and the other dermal vessels, while sarcoidosis is a variety of this reaction all being related through some form of tuberculous allergy.

If this were so it is remarkable that Eales's disease is so rarely associated with erythema nodosa — although the association has been recorded (Donders, 1958) — and it is surprising that Eales's disease presents so often in otherwise healthy young individuals, and, unlike erythema nodosum and sarcoidosis, is not typically associated with raised and abnormal serum globulin levels (Doden and Pieper, 1959), nor does it show the same prompt response to cortisone therapy. These are puzzling aspects.

OTHER INFECTIONS

If one accepts the thesis that Eales's disease is due to a tuberculous hypersensitivity then I think one must also be prepared to concede that other antigens might equally well initiate such a reaction, as originally proposed by O'Malley (1944). The evidence in the literature certainly suggests this to be the case for retinal vasculitis has been reported in a wide variety of unrelated diseases, such as brucellosis (Puig Solanes and others, 1953; Foggitt, 1954; White, 1961), torulosis (Beck and others, 1955), infectious mononucleosis (Jones, 1954), Rickettsia (Fontan and Barbancon, 1960), and or the virus of Behcet's disease (Bouzas, 1957), syphilis (Finnoff, 1921), leprosy (Landau, 1961), toxoplasmosis (d'Aron, 1959), and even focal infection has been suspected (Knapp, 1935; Moffatt, 1946; Werner, 1946). Incidentally such an association with a variety of diseases due to infective or toxic agents is true also of erythema nodosum (Perry, 1944). It is interesting that all of these conditions are infections, bacterial, spirochaetal or

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PERIODICAL VIBRATIONS ON THE ELECTROMYOGRAM OF THE EXTRAOCULAR MUSCLES

KUBOKI TETSUYA and DOMON EMI (Japan)

Since 1953 electromyography of the extraocular muscles has been one of the studies in ophthalmology However basic information about these particular muscles has been lacking We will report here on some basic features of the electromyograph of these muscles especially the internal rectus

Fig 1 As an electrode a single needle electrode made of a steel wire with a diameter of 0 3 mm was applied It was insulated with paint made of synthetic resin except for the tip The needle usually was inserted into the muscle through the skin of the orbital margin This slide shows the needle having been inserted to examine the internal rectus

Fig 2 This figure represents three patterns of the electromyograph of an extraocular muscle The top recording shows single oscillations of a single motor unit It is obtained with a needle electrode having a very small naked area at the tip The middle recording shows an interference pattern which is recorded with a needle having a relatively large naked area at the tip The bottom recording was obtained by our own original method This periodical wave is the result of summation of single oscillations of many motor units The chief components of our method are firstly relatively large naked area on the needle secondly some distance between the muscle and the needle and thirdly high velocity of recording



Fig 1

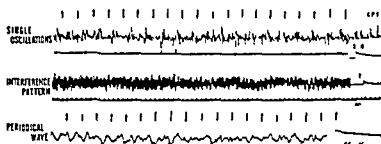


Fig 2

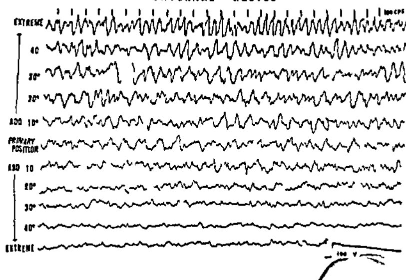


Fig 3

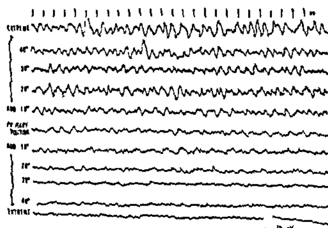


Fig 4

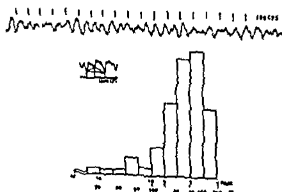


Fig 5

Fig 3 These recordings are the periodical waves of the internal rectus at various horizontal positions of the eye On the recordings are observed periodical vibrations which vary in frequency with the contraction of the muscle

Fig 4 These waves were obtained from the external rectus They resemble to a large extent, the waves of the internal rectu

Fig 5 The periodical waves were analysed by several methods Here I present one of the practical methods By measuring the length of each periodical wave a histogram of the frequency distribution of the waves with respect to the length or period of the waves was made



Fig 1

THREE PATTERNS OF EMG

(INTERNAL RECTUS)

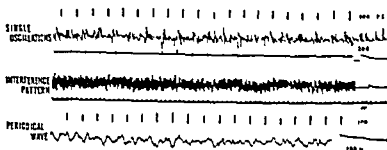


Fig 2



Fig 3



Fig 4

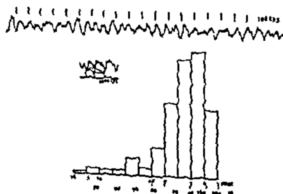


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Fig 1

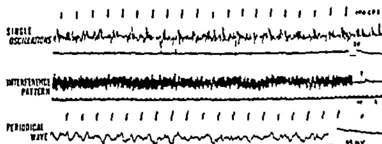


Fig 2



Fig 3

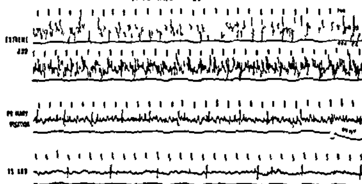


FIG 9

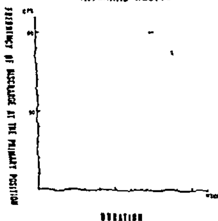


FIG 10

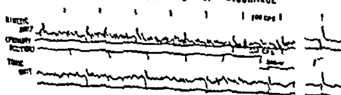


FIG 11

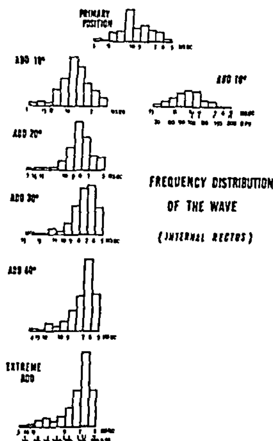


Fig 6

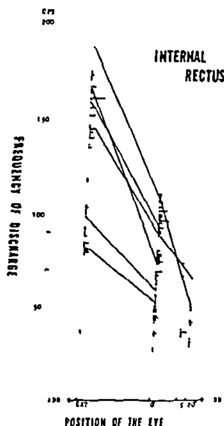


Fig 7

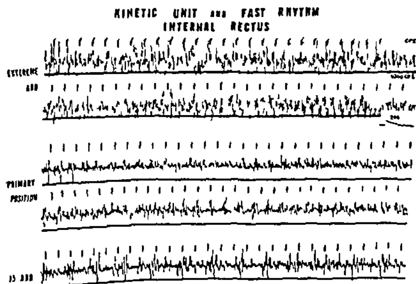


Fig 8

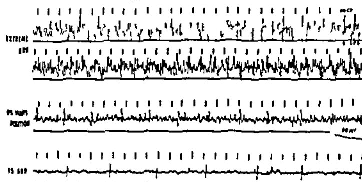


Fig 9

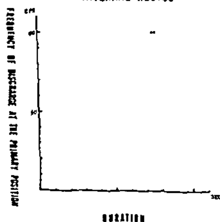


Fig 10

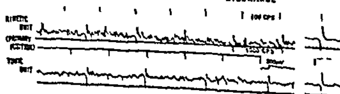


Fig 11

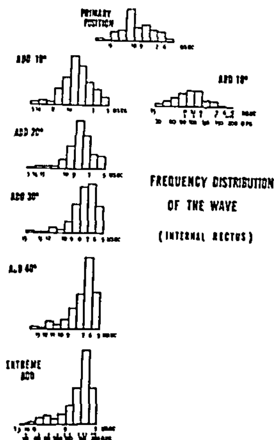


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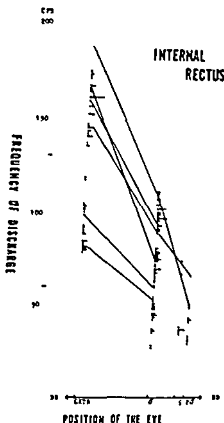


Fig 7

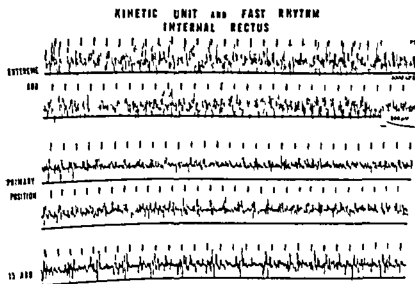


Fig 8

viral in which immune mechanisms are especially prominent and in which hypersensitivity is known to develop

ASSOCIATION WITH NERVOUS MANIFESTATIONS

There seems to be no doubt that retinal perivasculitis can occur in association with nervous manifestations — an incidence of 16 per cent has been quoted (Ballantyne and Michaelson 1948) The suggestion has been made that this is due to a coincidental periphlebitis of the cerebral vessels (Axenfeld, 1921 1927, 1930) and some of the conditions reported are apoplexy (von Graefe 1854) convulsions (Ballantyne 1909), transient paralysis (Lowenstein, 1931) polyneuritis (Duvoir and Bernard 1933) epilepsy (Haverkorn van Rijewijk, 1938) paraplegia (Silfverskiold, 1947) and severe headaches (Veirs, 1948) but most notably it has been described in association with multiple sclerosis (Ter Braak and van Herwaarden 1933 Rucker 1945 1947, Haar 1948 1949 1953 Wybar, 1952 Gougard and Paris 1954 Hagedoorn 1955 Orban 1955 Paufique and Etienne 1955 Shubova and Konchakova, 1957) in which disease retinal periphlebitis has a reported incidence varying from 10 to 40 per cent (Donders 1958)

It is questionable, however whether many of these cases should be considered in the category of Eales s disease since predominance in the male sex was not always a feature and retinal haemorrhages and retinitis proliferans were frequently absent Moreover as suggested by Jefferson and Cloake (1952) there is the possibility that the retinal and neurological manifestations may co exist by chance It is of interest that recent clinical investigations have obtained contradictory evidence Thus Silfverskiold (1947) reported 22 and Jefferson and Cloake (1952) six typical cases of Eales s disease showing no evidence of neurological involvement whereas White (1961) found neurological disorders in seven of 17 typical cases Conversely Donders (1958) found no evidence of retinal vasculitis in 25 cases of multiple sclerosis whereas Scott (1961) found sheathing of the retinal veins in seven of 65 cases

The most recent view is that of White (1961) who maintains that the association is a real one and that the retinal vasculitis is a non specific inflammatory lesion which probably occurs in the vessels of the parenchyma and meningeal coverings of the brain and spinal cord According to him the fact that similar lesions may develop in the central retinal vein as originally shown by Ballantyne and Michaelson 1937) and by Verhoeff and Simpson (1940) and more recently by Lyle and Wybar (1961) merely emphasises the anatomical and functional continuity between the retina and the remainder of the central nervous system

Are we to assume then that Eales s disease is the retinal expression of a vasculitis which may affect the whole central nervous system? This is a crucial question which cannot yet be decided for it appears is often denied as supported Francois and Neetens (1959) in describing a characteristic instance of sheathing of the retinal veins in a case of

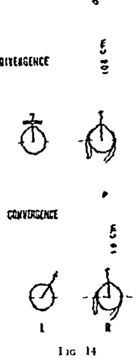


Fig 14

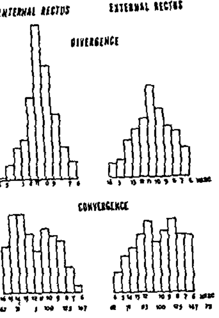


Fig 16

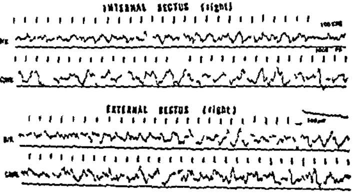


Fig 15

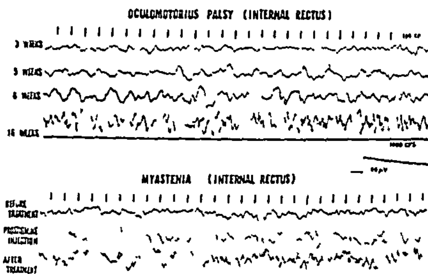


FIG 12

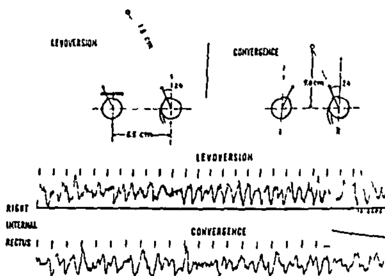


FIG 13

Fig 6 These are the frequency diagrams of the internal rectus corresponding to each horizontal position of the eye We can know that the waves of the primary position have a periodicity of about one hundred cycles per second, which increases in frequency proportionally to the contraction of the muscle, until a maximum of 160 cycles per second is reached at extreme contraction Furthermore on intense contraction of the muscle, there appears another maximum on the diagrams in the region around 90 cycles per second We designated the former the " fast rhythm ", and the latter the " slow rhythm' We must now confess that this explanation concerning the relation of

Fig 8 *This figure shows the single oscillations of the kinetic motor unit,* which gives rise to the fast rhythm at the extreme adducted position and also at the primary position

Fig 9 These are the samples of the tonic units This kind of unit gives rise to the slow rhythm, only in the intense contraction of the muscle We don t have much data on the external rectus but it seems to resemble the internal rectus to a high degree

Fig 10 This figure represents the relation between the duration and the frequency of discharge at the primary position of a single motor unit of the internal rectus It is conceivable that the kinetic unit has a high frequency and a long duration while the tonic unit has a low frequency and a short duration

Fig 11 The upper two recordings show the samples of a kinetic unit and tonic unit

Fig 12 In a case with oculomotor palsy abnormally slow rhythm was observed during the process of recovery In a case with myasthenia very irregular patterns were observed

Fig 13 The most interesting is the wave pattern of the internal rectus upon convergence The frequency of the rhythm on the wave decreases remarkably upon convergence, although the concerned eye does not change position

Fig 14 In order to investigate both horizontal recti it is advantageous to use the position of unilateral convergence

Fig 15 The waves of both internal and external rectus muscles of the resting eye revealed a decrease in rhythm upon convergence However it is less remarkable in the external rectus

Fig 16 The frequency diagrams of the waves indicate that the predominant rhythm of both recti becomes slower upon convergence

Fig 17 This phenomenon was confirmed by observing the activity of a single motor unit This recording shows one example of a unit of the internal rectus which decreases in discharge frequency upon convergence

Fig 18 On the other hand we can find occasionally some unit showing conversely higher activity upon convergence

Fig 19 These curves represent the changes of discharge interval of single motor units of the internal rectus Here we can find three types of unit The motor unit of the first type which decreases in frequency upon convergence, seems to belong to the kinetic group and to be the predominant one This would be related to the phenomenon that convergent movement is more limited than conjugate adduction The units of the second and the third type seem to be small in number and the relationship of them to the kinetic and tonic groups is not clear

Fig 20 Upon a divergent movement just the converse phenomena were observed

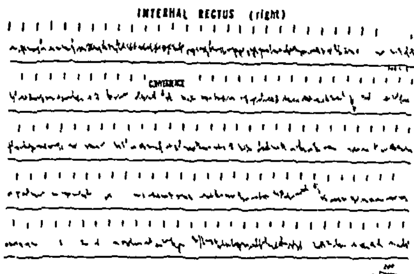


Fig 17

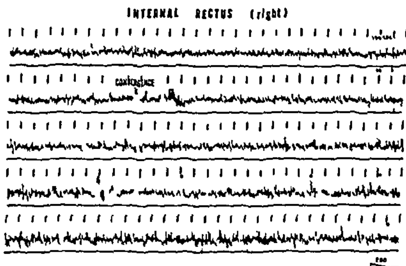


Fig 18

the two *rhythms is different from the one which was written in the* summary The reason will be clarified in the following data

Fig 7 This figure shows the frequency of discharge of single *motor units of* the internal rectus, in relation to the horizontal positions of the eye From the distribution of the points at the extreme adducted position, it is inferred that the motor units of this muscle are roughly divided into two functional groups The one group shows a frequency of discharge around 160 cycles per second while the other group around 90 cycles per second The former group is presumed to be the origin of the fast rhythm, and the latter of the slow rhythm We call them for convenience the 'kinetic unit' and the 'tonic unit'

Fig 8 This figure shows the single oscillations of the kinetic motor unit, which gives rise to the fast rhythm at the extreme adducted position and also at the primary position

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INTERNAL RECTUS

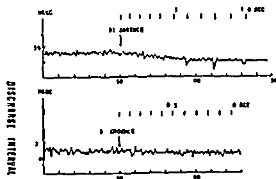
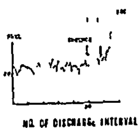


Fig 19



INTERNAL RECTUS

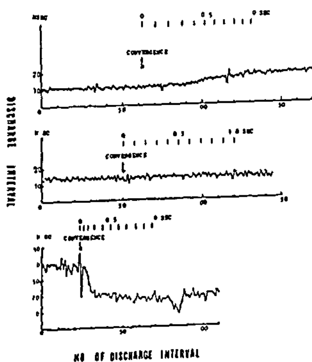


Fig 20

EXTERNAL RECTUS

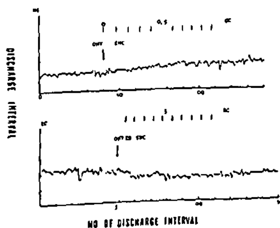


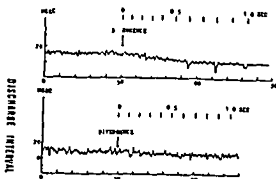
Fig 21

Fig 21 The external rectus, acted similarly to the internal rectus

In conclusion we found two functional types of motor units in the internal rectus and called them the kinetic and the tonic unit They are respectively the origin of the fast and the slow rhythm

Upon convergence, a decrease in frequency of the fast rhythm was observed and it was presumed that it was due to the decrease of discharge frequency of the kinetic motor units

The external rectus greatly resembles the internal rectus however, the details were not clear



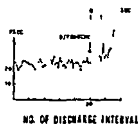


Fig 19

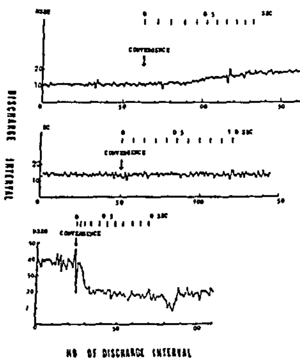


Fig 20

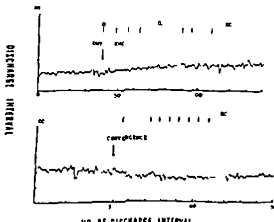


Fig 21

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multiple sclerosis believe that this *is not a true inflammatory reaction* but results from the accumulation and absorption of the disintegrating products of nervous tissue. A similar suggestion was made by Greenfield (1958) in the case of multiple sclerosis, although he postulated that the perivascular infiltration was secondary to the destruction of myelin, which of course *is not present in the retina, making the analogy* difficult to maintain. Moreover, it should be remembered that destruction of the retina in such diseases as diabetes, or in arterial or venous occlusion is not usually accompanied by an infiltration of inflammatory cells. In fact François and Neetens (1959) themselves pointed out *important differences between the fundus picture of Eales's disease* and the sheathing of the retinal vessels in multiple sclerosis; certainly the granulomatous type of reaction occasionally seen in Eales's disease has not been described in multiple sclerosis.

Nevertheless, it is possible that the occasional co-existence of Eales's disease and multiple sclerosis may be explained on an allergic basis, for recent research into the aetiology of the demyelinating diseases *is emphasizing to an increasing degree the possible role of* allergic factors by invoking an auto-immune reaction to neural protein, (Kabat and others, 1941; Ferraro, 1944). The relationship is not, however, a simple one for brain tissue antigen alone is unable to produce experimental demyelination and in some way requires the assistance *of infectious agents to form a complete demyelinating* antigen. It has been suggested, for instance, that experimental allergic encephalitis is elicited by neural protein as an anamnestic response in a co-existing but unrelated immune state, such as may be excited by tuberculoprotein or other bacterial or viral antigen (Lumsden, 1961) and it has lately been claimed that the *prominent demyelinisation* may itself be secondary to an allergic alteration in the biochemical characters of the small venous walls (Field, 1961). Here then may lie the connection between multiple sclerosis and retinal vasculitis.

OTHER AETIOLOGICAL CONSIDERATIONS

The original suggestion of Marchesani (1934a, b) that Eales's disease was a manifestation of thromboangiitis obliterans (Buerger's disease) was subsequently so discredited, particularly by Schmid (1945) who found no evidence of this disease in *25* patients with retinal periphlebitis, and no evidence *of retinal changes in 86 cases of thrombo*angiitis obliterans, that I think we should dismiss this possibility from consideration until more convincing supporting evidence is forthcoming.

If we are to learn, however, from the successful solution of disease problems in the past, it may be wise to break away *for a moment* from the main stream of contemporary thought and to ask ourselves whether Eales's disease is in fact an inflammatory condition at all. We know, for instance, that the clinical picture of retinal sheathing may not necessarily be inflammatory and that some pathological examinations of Eales's disease have *shown no inflammation* — even

SYMPOSIUM VI

INTERNATIONAL ORGANIZATION AGAINST TRACHOMA

INTERNATIONAL ORGANIZATION AGAINST TRACHOMA

PROF G B BIETTI

I am particularly happy to welcome the Colleagues that are gathered here for the occasion of the General Assembly of the International Organization Against Trachoma held parallel with the International Congress of Ophthalmology I send a particular greeting to our hosts the Indian Ophthalmologists so active in the field of trachomatology and to the representatives of WHO whose regional office for South East Asia facilitated our presence to the actual Conference organizing the trachoma meeting just before the Congress itself

The number and the importance of the papers to be presented gives testimony that trachoma still aroused a great deal of interest among the ophthalmologists They are the best confirmation for the existence of our Organization which co operates with the League Against Trachoma for the preparation and co ordination of the scientific meetings and for the publication of the *Revue International du Trachome* The co operation with the League and the activity of Jean Sedan as General Secretary of both Organizations, allows to enrich our international meetings with investigations which are indispensable reviews on the various chapters of trachomatology The recent advances on the studies on trachoma opens new horizons to research and to its practical developments particularly in the fields of the problems of immunology prophylaxis and treatment These perspectives permit us to foresee a great interest for our future meetings

I wish to count on your collaboration and scientific support for the future and declare officially open the activity of our General Assembly held on the occasion of the XIX International Congress of Ophthalmology

THE PRESENT DISTRIBUTION OF TRACHOMA IN THE WORLD

G B BIETTI, M J FREYCHE, R VOZZA

(Report to the Meeting of the International Organization Against Trachoma, New Delhi, 1962)

The aim of this report, which has been already published in the third number of the R I T, 1962 is not only to study the present state of the distribution of trachoma in the world, but also to analyse the factors which have contributed to the spread of the disease and the reason of the geographical differences in the clinical picture The 200 pages of the report are divided in five chapters

The first chapter deals with *the evaluation of the possible rates of morbidity* as obtained by the compulsory declaration of cases, by the evaluation of the ophthalmologists in the endemic areas, by the hospital and dispensary statistics and by the examinations of students and recruits, sometimes by "roadside" sampling All the afore mentioned methods are susceptible to criticism and could give place to data which are far from the real trachomatous index of the whole population This can be obtained with satisfactory approximation only by means of a 'sampling survey" carried out on a statistically sound sample During the collection of data for the present report, it was noticed that the school index, once considered practically equivalent to the general one, could be much higher in relation to the widespread use of drugs active on the trachoma virus and to the increased tendency to spontaneous healing, particularly in the areas where trachoma shows a reduced diffusion and a milder course In all the forthcoming epidemiological surveys this point should be considered, having also been recommended in the last Conference on ocular contagious disease, held in 1961 at Istanbul under the auspices of WHO

In the following chapter (2nd) are reported *the epidemiological data as obtained from documents* kindly supplied by WHO, from recent papers on the subject and from personal communications of the ophthalmologists of the endemic areas

These data, which may be only approximately summarized because of the non homogeneous diffusion within the same country, demonstrated that trachoma still maintains in the world a widespread although irregular distribution which does not differ considerably on the whole, from that reported by MacCALLAN in 1936

The affected areas may be therefore classified as follows

(1) Areas where the majority of the population is affected

Egypt Lybia Arab Palestine, Erythrean highlands, Kuwait and some districts of Tunisia, Algeria Morocco, Syria Lebanon Iraq, Iran Saudi Arabia Northern India, Viet Nam and China

(2) Trachoma highly widespread (trachomatous index with variable rates from 20 to 50 %)

Sudan Tunisia Algeria Morocco, Syria, Lebanon Iraq Iran Jordan Aden Southern Turkey Afghanistan South Viet Nam Laos Cambodia, Continental China India (areas), Indonesia, Borneo Thailand West Pakistan, Burma Equatorial East and South Africa (among the native populations)

(3) Trachoma quite common (trachomatous index 1 to 20%)

Mediterranean coasts of Spain Portugal Southern Italy Mediterranean Islands Greece Poland Hungary, Balkan States Rumania Bulgaria Southern and Central Russia Lebanon, Central and Northern Turkey Israel India (areas) Ceylon Korea Pacific Islands, Japan Pakistan Australia (among the aborigines) United States (among the American Indians), Argentina, Brazil Mexico New Zealand (among the Maoris) West Africa

(4) Sporadic cases of trachoma

Central and Northern Italy Finland Baltic States Sweden Ireland France (imported cases only) Philippines, Chile Guatemala Honduras Panama, Paraguay, Peru Salvador, Uruguay, Venezuela U S A (non Indian populations)

(5) Trachoma practically extinct

Switzerland Austria Germany Holland, Belgium, England and Scotland Denmark Norway Iceland and Canada

The present state of distribution of trachoma demonstrates that generally decrease of the trachomatous index took place reports of its increase being mostly related to better epidemiological information

It was observed that trachoma is in the place of extinction in Europe Infective centres are only present on the Mediterranean coasts (Spain Southern Italy Greece) and Islands (Sardinia Corsica Sicily Crete Greek Islands) in Portugal in the Balkans (Yugoslavia, Hungary) in Southern Russia

Substantial reductions of the trachomatous index were obtained among the African and Asian countries with very high contamination only in Morocco Tunisia Algeria Japan and to a lesser extent in Eritrea and South Africa

A very efficient control brought the disease to the extinction among the white population of the U S A where also the morbidity among the Indians is considerably reduced

Relying on these data an analysis was carried out in chapter 3, on the *factors suitable of determining differences in the clinical picture of the disease in the world* The authors have studied the influence of the

historical events which had an influence in this respect, as great migrations, military events (wars of conquest, transfers of garrisons) reasons of trade and migrations of workers

The importance of these phenomena has been discussed in detail as well as the local factors having enhancing or inhibitory activity on the spread of trachoma These were divided as follows

(1) Factors related to the individual,

(2) Ecological or environmental factors,

(3) Factors related to the properties of the infectious agent,

In the first group (factors related to the individual) the authors considered the importance of age, sex, race organic, previous or concomitant general diseases, diet immunitary condition (immunity and allergy), and of the preexisting or concomitant diseases of the ocular apparatus

As to the importance of the ecological or environmental factors they are considered to be of epidemiological interest, metereological conditions, personal hygiene, habits, religious practices, cultural and social level, professions, density of population, local environment and the possible vectors of the virus

As to the last group (properties of the infectious agent) it was noticed by the AA that the isolation of trachoma virus in the 5 continents will certainly clarify the importance of this problem

At the present time however in spite of the evidence of at least two antigenic viral prototypes, the importance of this laboratory finding has not been fully evaluated

The following chapter (4th) deals with the *geographical differences in the clinical picture of trachoma* The discussion of this problem is made difficult by the fact that the data referred to in the literature can hardly be compared because of the great disparity in the criteria used in the evaluation and in the collection of the clinical data

It can be stated however that, considering individually the trachoma cases no peculiar characteristics can be found in different places

Differential geographical characteristics can be established only by taking into consideration some of the clinical features of the disease as the age of onset, the appearance of scarring, the importance of the conjunctival hypertrophy, the presence and extent of corneal involvement, the presence of trichiasis etc

A typical difficulty in comparing the data of the literature in this respect is however demonstrated when one finds it practically impossible to evaluate the data concerning the corneal pannus since no agreement has ever been reached, even on the definition of this lesion

More reliable being less liable to errors or disparity of opinions in its evaluation, are the data relative to the incidence of entropion

trichiasis, with which it is possible to obtain an index of severity of trachoma not only geographical, but also for the same area in successive examinations

From the evaluation of this index, as well as others of the same reliability it was possible to demonstrate that the decrease of the trachomatous index is almost constantly preceded by a decrease of the incidence of complications and of disabling sequelae

From a general point of view, it was possible to conclude that the factors capable of inducing geographical differences in the clinical picture of trachoma can be grouped as follows

(1) Age of onset,
(2) Association with other kinds of conjunctivitis, mainly of bacterial origin,
(3) Degree of endemicity in the area,
(4) Hygienic habits and infectivity of the individual environment,
(5) Climatic factors,
(6) Properties of the viral agent
(7) Economical and social factors
(8) Therapeutic treatments carried out in the area
(9) Race
(10) Mode of transmission

Out of the aforementioned factors particularly important are believed to be the age of onset and the degree of endemicity which are however likely to influence each other Equally important are the incidence of bacterial superimposition and the socio economic conditions of the environment Although it can not be ruled out, the influence of the race is now considered with less attention

It should be noted however, that all the aforementioned factors cannot be considered singularly in their activity since they are frequently present at the same time in the area and they tend to influence each other in giving place to the particular features of the disease in a certain district

As to the distribution of the blindness due to trachoma the following conclusions were reached

(1) The incidence of blindness is directly proportional to the level of endemicity
(2) No racial groups are spared by the blindness that result from trachoma
(3) The incidence of blindness is conditioned not only by the degree of contamination of the area but also by the activity of the same factors which are capable of rising the severity of the disease like bacterial infection socio-economic, under-development etc.

In the last chapter (5th) an analysis of the *causes of the decrease of the trachomatous index* in certain districts, was carried out

This problem was studied in the countries where reliable data on the prevalence of trachoma were available for the last 60 years, i e the European countries, the U S A and Japan

A particular attention was devoted to the evolution in the behaviour of the disease in Italy where in this period trachoma was brought to extinction in the Central and Northern districts, while a considerable number of cases are still present in the South and Islands This different diffusion was related to the mass and school campaigns regularly carried out during this period and to the considerable improvement in the standard of living This phenomenon, particularly evident in the Central and Northern districts, undoubtedly contributed considerably to the decreases of the trachomatous index

EFFECT OF TRACHOMA WITH LEDERKYN ACETYL INTRAMUSCULARLY INJECTED

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The structure of Lederkyn Acetyl, 3 (N 1 Acetylsulfanilamido) 6 methoxypyridazine is as figure 1 This compound was the out come of the research conducted by Medical Research of Lederle Laboratories Pearl River New York in 1958 This medicine belongs to one of the repository (slowly absorbed or slowly eliminated) sub stances which show an intensive inhabitive effect not only to strepto coccus staphylococcus pneumococcus, meningococcus, gonococ cus colibacillus dysentery bacillus proteus vulgaris but also to sulfaresistant viru es

According to the reports of Bietti (1959) and Wong (1961) Lederkyn used orally has given excellent results in the treatment of trachoma Lederkyn Acetyl is the 25 % suspension which can be applied intramuscularly This new medicine was kindly put at our disposal by Lederle Laboratories Our experiment is carried out on ten trachoma patients whose results and side effects are reported as under

MATERIALS AND METHODS

Ten trachoma patients three men and seven women, ranging in age from 14 to 48 and in weight from 40 to 56 kg, were given intramuscularly 5 to 7 times at intervals of 7 days The severity of trachoma was all mild being Tr I to Tr IIb under the McCallan classification

RESULTS

Course of the trachoma symptoms Decrease in conjunctival hyperemia was observable after the admini tration of the third injec tion and was still more remarkable after the fifth injection From about this time onward papillae and follicles were evidently on the decrease One month after the last injection pronounced improvement on the conjunctival findings were evident with papillary hypertrophy and formation of follicles left in almost none of the cases though in only one case a mild degree of papillary hypertrophy was still to be noted as shown in table 1 However this case was also completely cured in three months Improvement was less impressive against the pannus Twenty clinical findings before and after treatment are shown in figures 2 to 21 Scarcely any side effect was observed following intra

muscular administration of Lederkyn Acetyl. The renal function observed by 17-KS in urine before and after the injection is shown in figure 22. As in the figure there were no impaired symptoms. There was no variation in serum natrium and kalium levels as shown in figures 23 and 24. There was neither variation of the number of erythrocytes

TABLE I — *Course of Trachoma Symptoms after Injections*

Case No and Stage	*Initial Findings*		*At the 3rd Injection*	*One Month after the Last Injection*
1 Tr III	Conjunctival hyperemia	(+)	(→)	( )
	Papillary hypertrophy	(+)	(→)	( )
	Conjunctival scar	(+)	(+)	(+)
	Pannus	(+)	(+)	(+)
2 Tr I	Conjunctival hyperemia	(+)	(→)	( )
	Conjunctival hypertrophy	(+)	(→)	(→)
3 Tr IIb	Papillary hypertrophy	(+)	(+)	(→)
	Conjunctival hyperemia	(+)	(→)	( )
4 Tr IIb	Conjunctival hyperemia	(+)	(→)	( )
	Papillary hypertrophy	(+)	(→)	( )
5 Tr IIb	Conjunctival hyperemia	(+)	(→)	( )
	Papillary hypertrophy	(+)	(→)	(→
	Pannus	(+)	(+)	( )
6 Tr IIb	Conjunctival hyperemia	(+)	(→)	(→
	Conjunctival hypertrophy	(+)	(→)	( )
	Papillary hypertrophy	(+)	(→)	(
7 Tr III	Conjunctival hyperemia	(+)	(	( )
	Papillary hypertrophy	(+)	(+)	( )
	Conjunctival hypertrophy	(+)	(+)	(→)
	Conjunctival scar	(+)	(+)	( )
	Pannus	(+)	(+)	
8 Tr IIb	Conjunctival hyperemia	(+)	(—)	)
	Papillary hypertrophy	(+)	(→)	(→)
	Pannus	(+)	(+)	(+)
9 Tr IIb	Conjunctival hyperemia	(+)	(→)	(—)
	Papillary hypertrophy	(+)	(→)	(—)
	Pannus	(+)	(+)	(+)
10 Tr IIb	Conjunctival hyperemia	(+)	( )	(
	Papillary hypertrophy	(+)	(→)	(→)

Remarks (+) Positive reaction
(→) Decrease
(—) Disappearance

in the early stages (Elliot, 1954) Pathologically retinal perivasculitis is seen very commonly, yet Eales's disease is rare by comparison which makes one a little suspicious of there being any relationship

There have in fact been several suggestions that Eales's disease may not have an inflammatory cause French workers have particularly emphasized the role of endocrine factors (Mawas and Herschberg 1953) and others have pointed to defects in the haemopoietic system, such as anaemia (Cohen 1924, Rollet, 1930) hypoprothrombinaemia (Mawas 1945) or hyperthrombinaemia (Donner, 1953) polycythaemia (Litauer and Januszeweski 1934) or to some undiscovered blood deficiency (Hutchinson 1932), while a deficiency of essential fatty acids (Sinclair, 1956) or of Vitamin C (Zwiauer and others 1948) have been suggested

In recent years it has become apparent that peripheral lesions in the retina can result from entirely non inflammatory conditions which are all in some way attributable to circulatory embarrassment in the retina Peripheral haemorrhages for instance may occur in macroglobulinaemia from increased blood viscosity haemorrhages and neovascularization may develop in pulseless disease due to retinal hypotension and Eales's disease may be closely mimicked in sickle cell haemoglobin C disease as a result of chronic and recurrent vascular occlusion (Henry and Chapman 1954 Hannon 1956 Lieb 1957 Goodman and others, 1957)

None of these suggestions however has much support at the present time Kimura and others (1956) found no evidence of Vitamin C deficiency nor of hypoprothrombinaemia while electrophoretic analysis of the blood plasma showed no abnormal protein pattern Doden and Pieper (1959) carried out an electrophoretic study of the blood proteins in 94 cases of retinal periphlebitis and found no abnormality, whereas patients with multiple sclerosis showed frequent disturbances of the protein fraction Seidel (1955) could find no abnormality in the number and behaviour of the blood cells or in the coagulation processes and was thus unable to confirm the findings of Donner (1953) of a raised haemoglobin and erythrocyte value Lastly it should be noted that no microscopical evidence of an inflammatory vasculitis has been found in macroglobulinaemia or sickle cell haemoglobin C disease so that a non inflammatory concept of Eales's disease is at the moment untenable

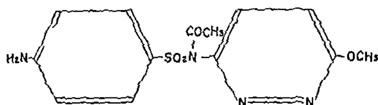
CONCLUSION

Our knowledge of the pathology of Eales's disease does not permit any final expression of opinion on its pathogenesis or aetiology but it may be generally agreed that retinal vasculitis particularly affecting the veins is probably the initial lesion

Vasculitis is a common pathological reaction in the retina and while in some cases the injury to the vessel walls may be due to the direct action of chemical or other toxic substances the majority are

as shown in figure 25 However, leukopenia was observed slightly by 4 8 % to 25 7 % as shown in figure 26

Fig I Structure of Lederkyn Acetyl



3 (N¹-Acetylsulfanilamido) 6-methoxypyridazine

Effect on Whole Body after Lederkyn Acetyl Intramuscularly Injected

Fig 22 17-KS in Urine

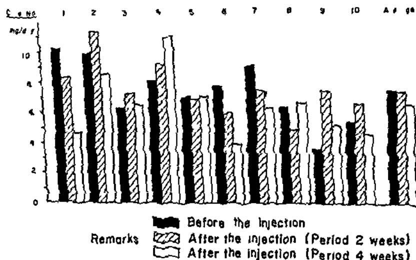
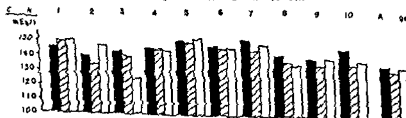


Fig 23 Natrium in Serum



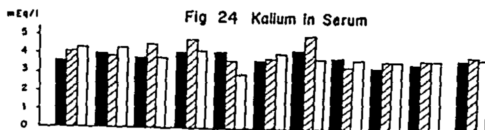


Fig 24 Kalium in Serum

See legend to Fig 22 for description

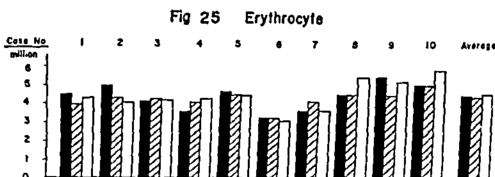


Fig 25 Erythrocyte

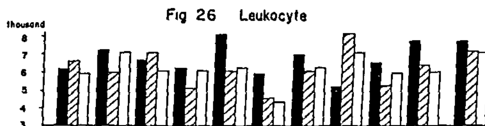


Fig 26 Leukocyte

See legend to Fig 22 for description

SUMMARY AND CONCLUSION

Lederkyn Acetyl intramuscularly injected has been established to give excellent effect in relieving mild trachoma Five doses of 6 cc at intervals of 7 days, have been proven sufficient There is no side effect upon the whole body Only leukopenia by 4 8 % to 26 7 % was noted in 3 cases

I wish to express my appreciation to Dr Ottati, Director of Lederle Laboratories Pearl River, New York by whom this paper was supported

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THE "COLLAR BUTTON" TECHNIQUE OF LID REPAIR

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Basal cell epitheliomata which do not involve the lid margin are usually handled by simple skin resection, sometimes the subjacent muscle is also taken However, once the margin or margin cum conjunctiva has become *involved* no matter how little it is customary to do a full thickness lid resection of the whole lesion This has always seemed a waste since the pathologic report in most cases shows no tarsal involvement

I should therefore like to present to you a new technique for the repair of lid epitheliomata which involve the lid margin or margin cum conjunctiva

This technique is based on two observations

1 The first observation is clinical Lid epitheliomata especially the basal cell usually start below the lid margin then spread slowly downward and upward to involve the margin and conjunctiva In a large percentage of these cases the marginal and conjunctival involvement is much less than that of the skin. Thus in a series of 91 cases of basal cell epitheliomata 39 cases showed marginal involvement and 14 also had conjunctival involvement The area of border and conjunctival involvement was considerably less than that of the skin

2 The second observation is pathological Serial sections of the lesions showed most or all of the skin layers involved The orbicularis was only rarely involved and then only in old long neglected cases No tarsal invasion was noted in any case even where the margin and conjunctiva were invaded This is not to say that it doesn t happen It probably does but if so it must be rare

One would think that the meibomian gland openings offer ready access to tarsal invasion by marginal neoplasms but this is not the case as repeated pathologic studies have shown

Based on these two observations the following technique of resection was evolved

Starting at the lid margin an incision is made through skin and muscle all around the skin lesion including 2 or 3 mm of healthy tissue Then starting at the margin again 3 mm to each side of the involved marginal (and conjunctival if involved) area two vertical incisions are made downward through tarsoconjunctiva These incisions

are curved in to meet each other below the tarsus in healthy conjunctiva. The ends of the skin muscle and tarsoconjunctival incisions at the border are united by incisions through the gray line (Fig A). The tissue thus outlined containing the whole lesion, the larger skin lesion and lesser marginal and conjunctival lesion, is split away from the rest of the lid en bloc (Fig B).



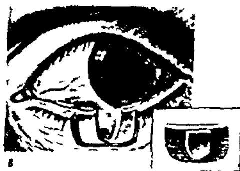


Diagram of halving by collar button resection technique

FIG A Lines of incision around lesion *Dotted lines* enclose tarsoconjunctival portion of lesion

FIG B Diagram of dehiscence left when the collar button shaped section (inset) is removed

Since the amount of skin muscle resected is always much more than tarsoconjunctiva, the resected portion resembles an old fashioned collar button and hence the name (*Fig B*). Many variations of this technique are possible of which a few are described.

1 A medium sized lesion involving the center of the lid corrected by a horizontal tarsoconjunctival closure and vertical skin muscle flap

In such a case a collar button resection is done as previously shown. With the help of canthotomy and cantholysis the tarsoconjunctiva is closed in the usual fashion.

Since the tumor is a shallow one, it is possible in such a case to fashion a vertical sliding skin flap, which is drawn up and sutured to the lid margin.

And here is a pathologic section through the centre of the lesion showing no tarsal involvement (*Fig C*).

2 In the case of a medium sized lesion at the canthus another variation in technique is possible.

Here repair is attained by means of horizontal closure of the tarsoconjunctiva as in the previous case. But the skin muscle lamina is closed by a temporal sliding flap thus taking advantage of the lesion's position. After a collar-button resection of the lesion a canthotomy and cantholysis permit closure of the tarsoconjunctiva.



Fig C Section through lesion of lid showing non invasion of tarsal glands

A temporal sliding flap is then fashioned which is pulled over the bared tarsus and sutured

Here again pathologic section showed no involvement of the tarsus

3 And finally when the lesion is large repair may be attained by a free whole skin graft

This lesion is resected collar button fashion and the tarso conjunctiva closed as in the two previous cases A free graft is taken from the ipsilateral upper lid and used to cover the dehiscence

The pathologic section shows involvement of the skin and muscle but the tarsus remained clear

DISCUSSION

In summary the collar button technique is suggested for (1) epitheliomata of the lid which (2) involves the lid margin or margin cum-conjunctiva and in which (3) the skin involvement is much greater than that of the margin (and conjunctiva) Wheeler pointed out long ago that the tarsus is a low grade tissue which heals poorly Perhaps this also accounts for its failure to be involved in neoplasms But however the case replacement of this inelastic relatively avascular tissue is not always easily accomplished Any procedure therefore, which minimizes tarsal loss facilitates lid repair Since the collar button technique reduces the amount of tarsal resection considerably one is frequently enabled to close the tarsoconjunctival wound directly thus avoiding tarsal grafting if one were to use the usual old techniques

Of course *this technique* will not be used in *old* neglected lesions in which the tarsus *may* be involved Also it is important to make sure that there has been complete excision of the neoplasm This is not difficult if sufficient healthy tissue is taken all around as described previously Furthermore this is always ascertainable by frozen section

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BOUTON D'ORIENT SIMULANT UNE DACRYOCYSTITE

A. MOTOLESE

Deux raisons importantes nous ont poussé à publier l'histoire de ce cas clinique, et tout d'abord la difficulté du diagnostic qui retarda passablement l'institution d'un traitement adéquat, puis aussi la rareté, voire la singularité, de ce cas dans notre région (Sud Est de l'Italie), jusqu'ici considérée zone exempte de maladies tropicales.

DESCRIPTION DU CAS

I. O., de Tarente (Italie) — femme de 60 ans, mariée à un officier de marine.

Six ans auparavant son oeil gauche s'étant mis à larmoyer, la patiente avait été soumise à de fréquents autant qu'inutiles sondages du canal lacrymal.

Plus tard une dacryocystectomie. Après l'opération la cicatrice resta granuleuse en dépit de l'application de traitements variés.

C'est dans ces conditions que la patiente se présenta à notre observation en septembre 1960.

EXAMEN OBJECTIF

O.D. = normal en toutes ses parties.

O.G. = bulbe oculaire normal en toutes ses parties. Dans la région du sac lacrymal une zone de teinte plus foncée, d'aspect granulé et semée de petites croûtes de sang. Le tout a la forme et les dimensions d'une grosse amande à pointe tournée vers le bas, limitée par la paupière supérieure vers le haut et par la partie latérale du nez vers *le bord droit; le pôle inférieur atteint presque la pommette gauche.*



due to an allergic reaction involving a wide variety of antigens The vessels may become sensitized through an intraocular antigenic source (lens protein, uveitis) or from an extraocular source (pulmonary *tuberculosis*, *brucellosis*), or possibly from the formation of complex autoantibodies as in multiple sclerosis

Eales's disease is one clinical form of retinal vasculitis, usually of unknown aetiology and characterised by recurrent peripheral haemorrhages in young males The two terms of Eales's disease and retinal vasculitis should not be used synonymously Regarded in this way it is not surprising that Eales's disease may have multiple causes or that it *should sometimes* present with vasculitis elsewhere in the retina or nervous system or with other allergic manifestations in the uvea or in the body generally

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La palpation révèle une consistance molle élastique

Le bord de cette formation, assez net vers l extérieur, est irrégulier vers l intérieur et légèrement détaché du fond à pic Le tout peut être assez facilement déplacé sur les plans profonds, malgré l opération précédemment subie

Frottée avec un tampon la surface s'effrite par petits fragments squameux et le fond, mis à nu, saigne en nappe

Une palpation plus énergique provoque l écoulement d une bonne quantité d un liquide muco-séro sanguinolent

Il est à remarquer toutefois que toutes les manœuvres auxquelles la lésion a été soumise n ont jamais provoqué aucune douleur chez la patiente

EVOLUTION

On décide de procéder à une nouvelle démolition du sac lacrymal et, par la même occasion de prélever un fragment de tissu en vue d un examen histologique car nous avions déjà émis l hypothèse d une affection chronique spécifique dont il restait encore à déterminer l agent

Avant l opération on prélève aussi en toute asepsie une goutte de la sécrétion du fond de la lésion on en fait un frottis que l on colore au Giemsa

La dacryocystectomie révèle la présence d un sac assez bien reformé et pourvu de péricyste presque normal

L évolution successive est caractérisée par une première phase de cicatrisation apparente rapide après laquelle la région du sac reprend son aspect primitif et l ulcération de la plaie opératoire s étend derechef en tous sens jusqu à regagner es anciennes limites et présente les mêmes caractéristiques morphologiques que la lésion précédente

Entre temps un fragment de tissu prélevé au cours de l opération ainsi que notre frottis coloré avaient été envoyés au Laboratoire d histologie de la Section d anatomie et histologie pathologiques dirigée par le Prof Dr Garau à l Hôpital provincial de Brindisi

Enfin voici le rapport que nous avons reçu du Laboratoire

BIOPSIE N 2207

Détails techniques fixation à l alcool inclusion dans la paraffine coloration hématoxyline eosine van Gieson

Histologie fragment de peau à épiderme d épaisseur irrégulière présence de tissu granuleux disposé de prévalence *en îlots* Les îlots sont formés d éléments épithélioïdes grands ou petits, auxquels se joignent des cellules géantes aux caractères semblables tantôt à des cellules de Langhans tantôt à des cellules géantes de nature irritative

Diagnostic histo pathologique tissu granuleux rappelant le tissu tuberculeux (Bouton d Orient)

BOUTON D'ORIENT SIMULANT UNE DACRYOCYSTITE

A. MOTOLESE

Deux raisons importantes nous ont poussé à publier l'histoire de ce cas clinique, et tout d'abord la difficulté du diagnostic qui retarda passablement l'institution d'un traitement adéquat, puis aussi la rareté, voire la singularité, de ce cas dans notre région (Sud Est de l'Italie), jusqu'ici considérée zone exempte de maladies tropicales.

DESCRIPTION DU CAS

F. O., de Tarente (Italie) — femme de 60 ans, mariée à un officier de marine.

Six ans auparavant son oeil gauche s'étant mis à larmoyer, la patiente avait été soumise à de fréquents autant qu'inutiles sondages du canal lacrymal.

Plus tard une dacryocystectomie. Après l'opération la cicatrice resta granuleuse en dépit de l'application de traitements variés.

C'est dans ces conditions que la patiente se présenta à notre observation en septembre 1960.

EXAMEN *OBJECTIF*

O. D. = normal en toutes ses parties.

O. G. = bulbe oculaire normal en toutes ses parties. Dans la région du sac lacrymal une zone de teinte plus foncée, d'aspect granulé et semée de petites croutes de sang. Le tout a la forme et les dimensions d'une grosse amande à pointe tournée vers le bas, limitée par la paupière supérieure vers le haut et par la partie latérale du nez vers le bord droit. Le pole inférieur atteint presque la pommette gauche.



(PERGOLA)

Les lésions du lupus peuvent aussi presenter des caracteres analogues la il faut alors se souvenir que leur evolution est bien plus lente que celle du Bouton d Orient de plus si l on appuie d une lamelle de verre, sur la peau envahie par le lupus on voit apparaitre des taches et des stries dont la teinte rappelle la couleur de la marmelade de pommes

(AGNELLO)

Certains caracteres peuvent aussi faire prendre le Bouton d Orient pour le xeroderma pigmentosum surtout dans la periode de l evolution cancereuse de ce dernier car c est a ce moment que l on trouve des formations verruqueuses avec erosion plus ou moins ulcerees Mais dans ce cas aussi l anamnese l evolution ainsi que les caracteres morphologiques plus particuliers nous portent vers une juste differenciation

Dans la litterature nous trouvons aussi des cas de Bouton d Orient qui par leurs caracteres morphologiques rappellent les verrues ou les cheloides Parmi les cas decrits par BEHDJET il y en a qui simulaient le lupus pernio l hémangiome et la tuberculose ulcereuse

HIGOUMENAKIS dresse une liste tres claire des multiples aspects cliniques presentes par le Bouton d Orient et qui peuvent le faire facilement prendre pour un impetigo un lupus une forme de tbc cutanee ou meme pour une affection verruqueu e eresypeloide furonculeuse etc

MONACELLI decrit encore d autres formes cliniques atypiques de Bouton d Orient rappelant surtout le lupus pernio et le lupus tumidus

MORETTI parle d un cas dont le tableau clinique simulait une affection épitheliomateuse

Quant au diagnostic differentiel entre le Bouton d Orient et un processus cancereux c est encore l examen histologique d un fragment de tissu qui sera le plus utile sans negliger l inoculation d un *fragment sous la peau ou dans l oeil* d un animal de laboratoire

D autre parteles caracteres d une manifestation mycosique peuvent etre pris par certains details pour un Bouton d Orient car il n e t pas *rare de trouver d*ans une affection mycosique un nodule arrondi et proeminent souvent ulcére entoure d une zone d infiltration pale, pourtant dans ces cas aussi un examen bacteriologique nous permettra d isoler le champignon enecause Le laboratoire est en effet d une *extreme utilite* pour arriver a une exacte differenciation de diagnostic au moyen de la recherche des micro organismes ou des éléments spécifiques dans les produits de secretion de l ulcere souvent à la recherche bacteriologique il faut encore ajouter l examen histologique d un fragment preleve a la lésion ainsi que l inoculation de celui ci sous la peau ou dans l oeil d un animal de *laboratoire*

Le resultat de l'examen du frottis etait le suivant on remarque la presence de corpuscules ovoides ou spheriques de 1 a 2 *microns* de diametre, entoures d'une mince membrane, protoplasme hyalin colore en bleu pale sans vacuoles, noyau excentrique colore en rouge

Conclusions Leishmania tropica ou corpuscules de Wright

A la suite de ces constatations un traitement au Stibosan (tartre stibie) a ete immediatement institue à raison d'une ampoule de 5 cc deproduit i m tous les trois jours En depit d'une certaine intollerance au medicament (quelques modiques manifestations d'intoxication), le traitement a pu etre prolonge pendant deux mois environ

La derniere fois que nous avons revu cette patiente — deux mois apres le debut du traitement — la lesion etait nettement en bonne voie de guerison et ne presentait plus qu'une petite ulceration centrale entourée d'une vaste zone de reepithelialisation a bords minces et plats

PERGOLA DIT QUE

Objectivement parlant du point de vue de la clinique et d'apres ses caracteristiques macroscopiques, le Bouton d'Orient peut fort bien se preter comme sujet de discussion quant au diagnostic differentiel entre des affections de nature differentes et l'on pourrait aussi, comme dans le cas ci dessus, se poser la question s il s'agit d'un processus de neoformation d'origine inflammatoire ou d'origine neoplasique, ou bien d'une manifestation mycosique

Pour le diagnostic differentiel il faut se souvenir que parmi les nombreux processus inflammatoires se trouvent en premier lieu les processus chroniques specifiques syphilis et tbc La syphilis, notemment, peut provoquer des ulcerations et meme des gommes comparables, a certains moments du moins, aux lesions dues au Bouton d Orient Toutefois les caracteristiques essentielles de l ulcere syphilitique sont en premier lieu son evolution rapide, puis l aspect particulier des bords et de la base et surtout l'adénopathie qui accompagne constamment cette affection L'engorgement des ganglions preauriculaires et sous maxillaires est, en effet, constant dans la syphilis tandis que l on ne trouve presque jamais cette manifestation dans le Bouton d Orient

Au cas ou l on serait porte a soupçonner une manifestation tuberculeuse la clinique pourra toujours, par exclusion, fournir de precieuses indications Dans l ulcère tbc il n est pas rare de trouver de veritables granulations miliaires et, plus frequemment, de petits ilots blanchatres caseeux et des ulcerations parfois tres profondes et penetrantes qui detruisent rapidement une grande partie des tissus profonds Il est vrai que certains de ces caracteres cliniques se retrouvent meme dans la Bouton d Orient, mais la lenteur de l evolution de ce dernier est toujours là pour nous mettre en garde quant a la veritable nature de l'affection

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Au cas où l'on serait porté à soupçonner une manifestation tuberculeuse, la clinique pourra toujours, par exclusion, fournir de précieuses indications. Dans l'ulcère tbc. il n'est pas rare de trouver de véritables granulations miliaires et, plus fréquemment, de petits îlots blanchâtres caséeux et des ulcérations parfois très profondes et pénétrantes qui détruisent rapidement une grande partie des tissus profonds. Il est vrai que certains de ces caractères cliniques se retrouvent même dans le Bouton d'Orient, mais la lenteur de l'évolution de ce dernier est toujours là pour nous mettre en garde quant à la véritable nature de l'affection.

RESECTION OF ORBICULARIS NERVE SUPPLY FOR INTRACTABLE BLEPHAROSPASM

ALSTON CALLAHAN, M D
903, South 21st Street *Birmingham Alabama*

In 1951 Sidney Fox described an operation for intractable blepharospasm consisting of removal of most of the orbicularis muscle His plan was used on the first patient who consulted us because of blepharospasm which had developed in part from repeated, excessive blinking from keratitis sicca and in part from having a highly nervous temperament

We removed part of the orbital orbicularis most of the preseptal part and some of the pretarsal part of the orbicularis muscle As the operation proceeded with the extensive removal of muscle tissue we feared that postoperatively the eye lids might not close but this fear was unjustified Though the blink mechanism was still active the amplitude and intensity of the sphincter action of the orbicularis muscles was reduced to a more normal level and the patient was benefitted

This massive removal of the orbicularis muscle was accompanied by oozing of blood from the muscle tissue and occasional spurting of the vessels required so much time and effort that we sought an easier way to improve such patients We then realized that if a sector of the lateral edge of the orbiculari was removed so that the nerve supply was partly disconnected that improvement might be achieved with less trauma to the patient and less effort by the surgeon

Our second patient with intractable blepharospasm developed this condition in part because of extreme photophobia from a slowly developing incipient cataract and he too had a highly nervous temperament

The technic About 8 to 10 cc of Xylocaine (R) Wydase (R) and epinephrine are injected along the antero-lateral angle of the face approximately 1 cm posterior to the canthal angle extending downwards vertically from the posterior edge of the eyebrow to the lower edge of the zygomatic bone

Fig 1) A curvilinear incision is made over the posterio lateral orbicularis border and a sector about 10 mm wide and 40 to 45 mm long of the muscle is excised exposing the periosteum beneath In severe cases a wider and longer sector of the orbicularis can be safely removed in one of our patients we removed all of the orbicularis lateral to a vertical line drawn through the lateral palpebral tendon

Il ne faut pourtant pas oublier que le seul fait de ne pas avoir trouve de micro organismes ne prouve pas nécessairement que l'affection ne soit pas specifique Dans le cas que nous venons de decrire, la recherche du parasite a ete assez laborieuse justement a cause des nombreux traitements et manipulations auxquels notre patiente avait ete soumise, bien que les caracteres morphologiques de l'affection cutanee et la presence de macrophages dans le frottis eussent du suffire a eux seuls a confirmer le diagnostic clinique Il faut, toutefois, etre circonspect et avoir toujours recours au diagnostic differentiel dans les cas ou l'examen bacteriologique serait negatif

RESUME

Description d'un cas de Bouton d'Orient dans la region du sac lacrymal gauche

Ce cas, deja interessant a cause de sa rarete, est le premier cas de Leishmaniose cutanee de la region du sac lacrymal qui ait ete jamais observe dans le Sud Est de l Italie

La grande variete de tableaux cliniques presentes par la Leishmaniose accroit encore l interet de ce cas au point de vue du diagnostic differentiel entre les nombreuses neo formations chroniques de nature specifique

Le diagnostic clinique a ete cobfirme par les resultats de la biopsie et des examens bacteriologiques

The skin can be united with interrupted or with a continuous suture of silk or Supramid Extra (R) (5 0) We prefer the latter because of its great strength and total lack of tissue reaction

The causes of intractable blepharospasm in our third and fourth patients were the excessive blinking with keratitis sicca in highly nervous patients Though our fifth patient had many neuroses and was under psychiatric care the technic as described has decreased the clinching ' effect of the orbicularis

DISCUSSION

Many questions were raised by members of the Congress as to the cause of intractable blepharospasm and whether there was danger of a complete paralysis of the orbicularis The causes of this condition are usually photophobia from various diseases keratitis sicca, and other conditions that cause frequent blinking all of the patients that I have een were high strung nervous personalities Orbicularis paralysis ha never occurred in our series

Dr Lester T Jones, of Portland Oregon kindly read over this article and has suggested a possible improvement of the method to control intractable blepharospasm He does not resect the muscle, but destroys the nerve supply He injects the local anaesthetic starting at a point approximately 25 mm lateral to the lateral commissure and infiltrates the subcutaneous area above and below this point An effort should be made not to get the anaesthetic *into the sub* muscular space A vertical incision is made through the *skin* and superficial fascia down to the muscle, extending above and below the point of injection The incision should curve slightly medially above and below and have a total length of 3 or 4 cm The muscle fibers are separated just enough to expose the submuscular fascia in which the facial nerve fibres are located The central 2 cm of the fascia i cut through exposing the bone and deep muscle fascia This should weaken the lateral half of the palpebral mu cles If more weakening is necessary *the patient* may be asked to squeeze the eye shut or a square wave or Faradic type bipolar stimulator may be applied to determine how far *above* and below the nerve fibers should be cut The nerve fibers that cause contraction of the medial ⅓ to ⅓ of the palpebral muscles should be *avoided It may* be possible in the upper part to bypass these fibers and then cut enough of the fibers going to the corrugator *to weaken its* action

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Fig 1 (Callahan) A curvilinear incision is made through the skin and subcutaneous tissues the posterio-lateral edge of the orbicularis muscle is exposed and a sector about 10 mm wide and 40 to 50 mm vertically is resected The sub-muscular fascia is not incised because the motor nerve supply lies between the muscle and the submuscular fascia Sometimes the nerve supply to the corrugator must be resected but the nerve supply of the frontalis should not be



Fig 2 (Callahan) A highly nervous patient had extreme photophobia from slowly developing cataracts and developed intractable blepharospasm To see he had to hold his lids and eyebrows up with his fingers

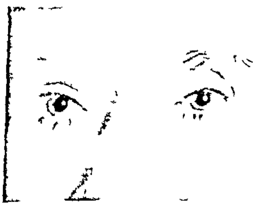


Fig 3 (Callahan) Six months after most of the nerve supply to the orbicularis was removed In none of our patients has too much orbicularis been resected for the patients have had no difficulty in closing their eye lids

It is unnecessary to remove tissue posterior to the orbicularis muscle and there is no danger of causing a facial paralysis if one does not extend the section further back than the orbicularis It is always surprising to see how much orbicularis contracture can still occur when a large part of the nerve supply has been disconnected

After the orbicularis resection, the subcutaneous tissues are drawn together over the defect and united with interrupted gut sutures (4-0)

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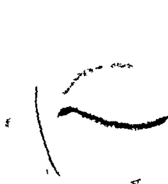


Fig 1

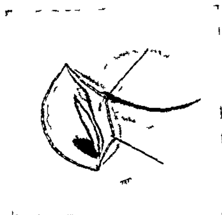


Fig 2

the periosteum in front of the anterior lacrimal crest the perio teum is widely separated from the bone to enable the tissues to be retracted by a few deep traction stitches The lacrimal sac enclosed in periosteum is mobilised laterally from the lacrimal fossa (Fig 2)

Every operation has its signposts and its rallying point Just as the anterior crest is the signpost for the lacrimal sac, so the medial palpebral ligament is the signpost for the common canaliculus and a traction stitch through its detached medial end is of great value whilst the dissection is deepened between the sac and the ligament by means of Rollet s rugine (Fig 3) As we have seen, this brings us directly down on to the common canaliculus with the least disturbance of the insertions of the important portions of the orbicularis on to the lateral surface of the posterior part of the palpebral ligament Care is needed because we are working through tough fibrous tissue down on to

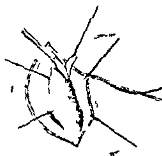


Fig 3

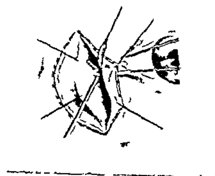


Fig 4

CANALICULODACRYOCYSTORHINOSTOMY

BARRIE R JONES

Institute of Ophthalmology and Moorfields Eye Hospital, *London*

Obstruction in the lacrimal canaliculi near the sac is fairly common, in London it probably accounts for 10% of epiphora requiring surgery (Jones, 1960) The literature records many attempts (Rycroft, 1960) but reveals no method of curing the condition with a degree of certainty approaching that given by the technique which I here present

AETIOLOGY OF OBSTRUCTION OF THE COMMON CANALICULUS

The two canaliculi often join together at their medial ends to form a short common canaliculus This passes medially through the posterior portion of the medial palpebral ligament and lacrimal fascia (Jones, 1957) to reach the lacrimal sac The appearance, relations and surgical behaviour of this little tube as seen in 10 operations upon it, leave no doubt that it is better described as a common canaliculus than as a sinus of the sac

In *primary stenosis*, which accounts for 32 of my 40 cases, the common canaliculus is squeezed by this tight fibrous tissue through which it passes to join the sac (Jones, 1960)

Acute, or occasionally chronic, dacryocystitis may lead to a *mucosal occlusion at the entrance of the common canaliculus into the sac*, as in 8 of my 10 cases

Mucosal obstruction of the common canaliculus was caused by irradiation in 2, erythema multiforme in 1, trachoma in 1 and conjunctivitis of unknown aetiology in another case

Traumatic avulsion of the common canaliculus also occurs at this site

THE TECHNIQUE OF CANALICULODACRYOCYSTORHINOSTOMY

My operation consists essentially of dissecting out the common canaliculus and a little of both upper and lower canaliculi removing any strangling fibrosis in the region of the medial palpebral ligament anastomosing the common canaliculus with the sac and completing the procedure with a dacryocystorhinostomy

The usual approach to the lacrimal sac is made through a straight incision well forward on the side of the nose (Fig 1) Bleeding points are picked up in non toothed dissecting forceps and rapidly coagulated by diathermy applied to the forceps The incision is deepened through

submucous resection of a portion of the middle turbinate, should it interfere large flaps of nasal mucosa can always be fashioned so that they will enable the sac to swing out laterally to make good the shortening resulting from the anastomosis of canaliculi to sac

Having cleared up any stray fragments of bone the sac is incised from end to end along its medial aspect (Fig 6) It is then swung medially and the common canaliculus is snipped off as close to the sac as possible If the obstruction extends far laterally it is necessary to incise down on to the probes but in any event the common canaliculus is slit along its upper and lower borders to form an anterior and a posterior flap Four Kalt silk sutures are passed on Jameson Evans or Grieshaber 82-5 needles one through each corner of the flaps of canaliculus These are passed through a short incision in the lateral wall of the sac the flaps of common canaliculus are pulled through on to the inside laid back and sutured to the mucosal surface of the sac (Fig 7) It is essential to completely mobilise the common canaliculus and sufficient of its tributaries to enable these flaps to be brought cleanly through inside the sac Often a few extra sutures are required to splay out the common canaliculus

In order to keep this anastomosis of canaliculus to sac cleanly open and lightly on the stretch with no possibility of it touching any other tissue I always combine it with a rhinostomy (Fig 8) Careful suturing of posterior and anterior flaps of the rhinostomy keeps the sac on the stretch from front to back and this is made more certain by hitching the sutures in the anterior flap forwards to the periosteum (Figs 9 & 10) Nothing is to be gained by leaving large catheters lying around in such a rhinostomy but it is my custom to pass one end of a fine polythene tube from the upper punctum through the anastomosis of canaliculus to sac and out through the nose and then to pass the other end similarly through the lower punctum This tube serves

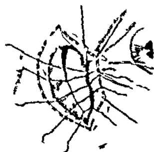


Fig 9

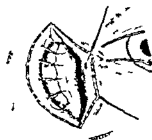


Fig 10

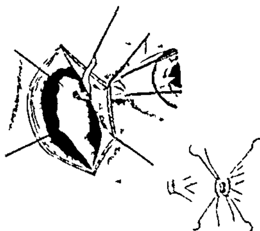


Fig 5

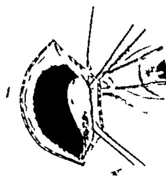


Fig 6

delicate tubes whose position is defined by having a probe in each canaliculus The mobilization of the common canaliculus is the rallying point of the operation but it is essential to separate this tube from the remaining portion of the ligament passing behind it to the posterior lacrimal crest (Fig 4)

At this stage I swing the sac laterally and proceed to remove the bone for the rhinostomy I remove a large area of bone extending forwards from the posterior crest to a point in front of the anterior crest and from about five millimetres above the fundus of the sac right down to include the party wall between nasolacrimal duct and nose (Fig 5) It happens to be my preference to use the Traquair separator followed by bone punches and nibblers and for some portions the gouge, because, in my hands at least, these are the most versatile tools By exenterating any obstructing ethmoid cell and carrying out

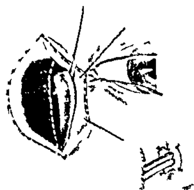


Fig 7

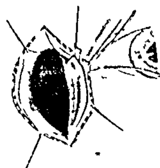


Fig 8

avoided This technique is applicable if the obstruction extends along one or both of the canaliculi for in this instance it is possible to anastomose either the upper or the lower canaliculus to the sac by splitting the little tube into an anterior and posterior flap (Fig 11) It is worth

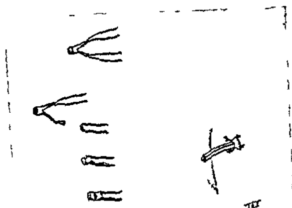


Fig 11

attempting if half of the lower canaliculus is patent Five out of six such cases have been entirely successful and it is especially gratifying to have cured two patients with the difficult post irradiational obstruction

SUMMARY

Obstruct on in the common canaliculus near the sac accounts for about 10 % of ep phora All but one of 40 cases have been cured by dissecting out these passages plitt ng the common canaliculus to form anterior and posterior flaps pulling these through an opening into the sac and suturing them apart inside the sac Careful suturing of the sac to the nasal mucosa completes the canaliculodacryocystor h nostomy

RESUME

I obstruction du canalicule commun pres du sac lacrymal est responsable d environ 10% des cas d épiphora A part une seule exception 40 malades ont ete gueris par la dissection des voies lacrymales la division du canalicule en deux lambeaux l un anterieur l autre postérieur que l on tire par une breche pratiquee dans le sac et la suture des lambeaux separement a l interieur du sac La canaliculodacryocystorhinostomie est completee en suturant avec soin le sac et la muqueuse nasale

ACKNOWLEDGEMENTS

In presenting this procedure I am indebted to Professor Rowland Wilson University of Otago N Z who first confronted me with the

merely as a splint whilst the surfaces are healing and I remove it after a week or two In closing the wound, it is important not to attempt to suture the palpebral ligament to the periosteum because having divided its deep attachment to the posterior lacrimal crest, the resulting pull forward and nasally may displace the puncta away from the globe

It is clear that what matters to the patient is what is done to him rather than what tools are used, but these two double dissectors, one being sharp and modelled after a Tooke s knife, straight and angled, and the other having a sharp rugine at one end and a semi sharp spoon at the other end, facilitate the dissection The suturing of these fine flaps of mucosa within a rather awkward and restricted field is considerably facilitated by a pair of angled crocodile needle holding forceps which Mayer and Phelps have made to my specification The needle can be held at any angle, the smooth surfaces are a delight in tying the knots and the unobstructed view it allows is a great advantage

POSTOPERATIVE MANAGEMENT

Until the polythene tube is removed after a week or two, Albucid drops keep the eye clean It is important to relieve postoperative nasal congestion and remove mucus and blood clot with Narist ephedrine ½% in normal saline twice daily until the nasal surfaces have healed cleanly The sutures in the anastomoses usually fall out within the first few months — if not I remove them through the nose

It is important to watch some cases carefully during the first three months Of 40 operations, 6 have shown a tendency to closure at the site of the anastomosis of canaliculus to sac With the gentle passage of probes this tendency was overcome in all but 2 After the third or fourth month the condition has remained stabilised

The only other point requiring attention has been a slight eversion of the lower punctum in half the cases during the first month This may be very easily overlooked unless the lid margin is examined from above with the patient looking up In 5 cases the cautery was required to correct the position of the punctum

DISCUSSION OF RESULTS

Thirty eight of the 40 operations have given completely dry eyes It is possible to repeat the canaliculus to sac anastomosis and in this way I have cured one of my failed cases, the other is awaiting admission for this

The operation has been in use for 7 years and no case which was initially successful has shown any tendency for late closure I believe that the two crucial points in the success of this procedure are the two points in which it differs fundamentally from alternative methods firstly the fibrous tissue that is strangling the canaliculus is dissected away, secondly by bringing the canaliculus into the sac and splaying its ends apart anything approaching an end to end anastomosis is

NEW TREATMENT OF PTERYGIUM

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The pterygium is possibly produced from the pinguecula which has degeneration of conjunctival connective *tissue due to acquired* stimulation from outside On this point, some investigators have the same opinion However the reason why the degeneration of connective tissue extends to the corneal connective tissue is unknown

The authors have an opinion that the focus of the pterygium is present in the head which has intensely degenerated mass of connective tissue as the pattern of figure 1 From the focus the degeneration advances further to the centre of the cornea In this process it passes between the corneal epithelium and the Bowman s membrane, and

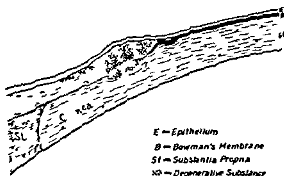


Fig 1

produces swelling or thinning or irregular curvature on the latter At last Bowman s membrane is destroyed and parenchymal fibres directly under the membrane show degeneration On the other hand, in regard to the limbal side the degenerated mass of connective tissue of the head has firm tendency to be repaired gradually by regenerated fibres due to propagated fibroblasts and invaded blood vessels On more close area to the limbus the corneal tissue regains completely its normal thickness and curvature although the Bowman s membrane is absent in the area. However the degenerated mass which is pushed out of the cornea is replaced by the conjunctival connective tissue

condition, to the Surgeons of Moorfields and the London Hospital who encouraged me to carry out this operation, to Miss M George for her help with the radiology and to Mr T R Tarrant and to our Department of Medical Illustration who prepared the illustrations

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removed No suture is placed In the procedure, attention must be placed on the following points

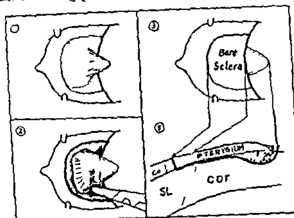


FIG 2

(a) To remove completely the head of the pterygium which has the degenerated tissue
(b) To expose the sclera completely by thorough striping and the removal of the body of the pterygium with Tenon's capsule from the sclera
(c) Degenerated mass in the cornea must be removed completely At this time, one must avoid excessive removal of normal corneal tissue Especially, on the limbus the removal is limited to the superficial layer as figure 2(3) in order to expect easy repair
(d) Normal conjunctiva which connects with the upper and lower borders of the pterygium must be removed Thick line on figure 2(1) shows the line of the removal When the defect of conjunctiva is too wide to be repaired, the line of removal must be put along the dotted line

The area of the wound due to the above procedure consists of the following parts They are the conjunctival area and the corneal area In regard to the former the conjunctiva is removed and the sclera is exposed on the area which spreads from the muscle terminal to the limbus In regard to the latter the lamellar defect which reaches the corneal parenchym is formed.

3 RESULTS OF THE OPERATION

On the next day of the operation on all cases the bare sclera is clear and dilated capillaries run on it Notable signs of inflammation are not observed The course which received thio TEPA instillation was as follows

After 3–4 days from the beginning of instillation, the surface of the wound is covered by fibrin mass (Fig 3) Afterwards with the lapse of days fibrin mass decreases and vascularization invades from

with blood vessels On the occasion, the latter becomes the same figure as that of the normal conjunctival tissue Afterwards, it occasionally takes on a cicatrice like feature by the occurrence of partial fibrosis

1 NEW TREATMENT OF THE PTERYGIUM

During the operation, it is advisable to remove the degenerated mass of the head, completely, because the source of the pterygium is the degenerated mass of connective tissue in the head

The procedure is important to prevent the recurrence In regard to the neck, the same care is needed, because a part of the degenerated mass is present in the cornea On more adjacent part to the limbus, where normal thickness and curvature of the normal corneal tissue are regained, degenerated mass is present in the conjunctiva like tissue which rides on the cornea Therefore, a single removal of conjunctiva like tissue is satisfactory

However, even when degenerated focuses are removed completely, the recurrence occurs when operative defect of the tissue is replaced by conjunctival granulation The most important procedure to prevent the recurrence is to inhibit the granulation which is produced on the wound of the conjunctiva Moreover, it is necessary to prevent the invasion of granulation into the operative defect of the cornea Recently irradiation with use of Sr [90] has been performed This method is adequate to meet the above condition When granulation does not invade the corneal defect, a natural regeneration of the cornea begins This process is slow, however, the defect is repaired Invasion of vascularization is not observed, on the occasion

To satisfy the above condition, the authors used thio TEPA and mitomycin C which are so called oncostatic preparations These preparations have the power to suppress the formation of granulation on the cornea and conjunctiva, and the effects are not inferior to Sr [90]

4 mg/ml thio TEPA diluted by physiological saline and 0 4 mg ml mitomycin C diluted by 5% glucose were prepared Instillation of these solutions were performed 3 times a day during 1–2 weeks after the operation The procedure of the operation is as follows

2 THE TECHNIQUE OF THE OPERATION

The authors performed bare sclera method As figure 2, apart 6–8 mm from the limbus, an incision is placed on the body of the pterygium along the limbus The incision is elongated and the body of the pterygium is cut Normal conjunctiva is exposed Horizontal incision is placed on the normal conjunctiva up to the limbus Lobe like body of the pterygium is striped from the sclera completely, with Tenon s capsule When the striping reaches to the limbus, a small piece of a razor which is snapped off to adequate size is picked up with a razor blade fragment holder as a sickle The blade of the razor is inserted under the lobe like tissue and advanced in the cornea from the limbus to the apex of the pterygium, as figure 2(2) Finally, the pterygium is

due to an allergic reaction involving a wide variety of antigens The vessels may become sensitized through an intraocular antigenic source (lens protein, uveitis) or from an extraocular source (pulmonary tuberculosis, brucellosis), or possibly from the formation of complex autoantibodies as in multiple sclerosis

Eales's disease is one clinical form of retinal vasculitis, usually of unknown aetiology and characterised by recurrent peripheral haemorrhages in young males The two terms of Eales's disease and retinal vasculitis should not be used synonymously Regarded in this way it is not surprising that Eales's disease may have multiple causes or that it should sometimes present with vasculitis elsewhere in the retina or nervous system or with other allergic manifestations in the uvea or in the body generally

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However when the tendency to form granulation is vigorous, granuloma is formed (Fig 5) and occasionally, then develops into a recurrence of the pterygium

Secondly the course of mitomycin C instilled cases is related During the interval from the 1st day to the 5th day permeation occurs on the surface of the wound and the surface becomes covered by fibrin mass Afterwards, the fibrin mass rapidly disappears Permeation is more slight compared with thio TEPA instilled cases But the tendency to form granulation is weak The surface of the wound takes the appearance of a normal conjunctiva after 20–40 days

The results of the operation on which thio TEPA or mitomycin C instillation was combined were illustrated on Table 1

Table 1

After Operat on (Months)	*Thio TEPA*		*Mitomycin C*	
	Total	*Recur*	*Total*	*Recur*
1 — 3	5	0	10	0
4 — 6	8	2	7	0
7 — 12	10	2	—	—
13 or more	8	1	—	—
TOTAL	31 (83 9%)	5 (16 1%)	17	0

Table 2

Days	KEEP IT 25 C — 30 C		
	Purity (%)	*pH*	*Appearance*
0	100 00	7 1	Uncolor almost transparent
10	98 81	8 65	
16	97 36	—	
21	93 65	8 65	Polymeric Compound partly precipitate
30	87 83	8 55	Polymeric Compound precipitate
60	66 89	8 5	
90	50 20	8 5	

Stability of aqueous solution of Thio-TEPA

the adjacent conjunctiva and the surface of the sclera Then, a partial granulation is formed

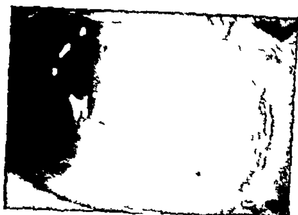


Fig 3



Fig 4



Fig 5

Afterwards, this process proceeds gradually and the surface of the wound is repaired from the periphery After a certain period, the granulation disappears gradually and the surface shows the same appearance as that of the normal conjunctiva (Fig 4) It takes 1–2 months to reach this state

is performed again and continued for a week For few obstinate cases instillation and Sr^{90} irradiation was combined

Instillation of thio TEPA or mitomycin C had no significant side effect However, the former provoked allergic conjunctivitis on 2 cases

CONCLUSION

The authors investigated the genuine nature of the pterygium by biomicroscopical and histological studies and found a new treatment The degenerated foci in the cornea, and the body and neck of the pterygium, were removed Bare surface of the wound was not covered Postoperative instillation of oncostatic preparations (Thio TEPA and Mitomycin C) gave favourable effects which were no inferior than the effect of Sr^{90} irradiation This method was very effective for the operation of recurrent pterygium and for aid in other conjunctival operations

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* Thio-TEPA = Tespamin (Sumitomo Chemical Co Ltd Higashi ku Kitahama 5–22 Osaka Japan)

N N N Triethylen Thiophosphoramide

Color of Crystal Colorless crystal or white crystalline powder

Molecular weight 189 22

Tentative molecular form $C_6H_{12}N_3PS$

Melting point 52–55 C.

Easily soluble Water Alcohol Ether Benzen Acetone Etheracetate

Sparingly soluble Petroleum ether

pH 6 5 (Aqueous solution 1 10)

Mitomycin C (Kyowa Hakko Kogyo Co Ltd Tiyoda ku Ôtemachi, 1–4 Otemachi Building Tokyo Japan)

Streptomyces caespitosus — 1956 T Hata — Fraction X

Color of Crystal Deep bluish violet.

Elemental Analysis C = 53 84 H = 5 14 N = 15 49

Molecular weight About 1 120 (When m-dinitrobenzene was used as solvent — Rast's method —)

Tentative molecular form C H N_4O_{14} (Calculated C = 54 22 H = 5 14 N = 15 22 O = 25 42)

Table 3

	pH	0	1	2	10	20 Days
5°C	7 0	100	100	98 5	82 6	56%
	8 0	100	88 9	99 0	82 2	88
27°C	7 0	100	90 6	—	71 5	—
	8 0	100	88 6	—	78 7	—
37 C	7 0	100	88 9	87 1	35 6	—
	8 0	100	91 8	94 5	84 5	—

Stability of aqueous solution of mitomycin C at each temperature at pH 7 0 and 8 0

DISCUSSION

The unique points of the authors operation are to expose the sclera widely and to leave bare part without any cover or implanted graft Generally, such procedure forms hard granulation on the surface and the granulation rapidly covers the surface, then, invades in the cornea Conjunctival granulation makes cicatrice and contraction in the future Indeed, the pterygium is produced again and the disturbance of ocular movement or convergent strabismus is provoked When oncostatic preparations are instilled, the formation of granulation is suppressed In the majority, the granulation is not formed Even when small granulation is formed, it disappears naturally Normal conjunctiva regenerates on the surface of the wound and the pterygium completely heals

On the occasion, the defect of the cornea and the conjunctiva gradually receives natural repair from their respective connective tissue cells and epithelial cells Vascularization into regenerated conjunctiva is very slow

When thio TEPA and mitomycin C are compared to each other, the former gives more intense stimulation on the surface of the wound than the latter Consequently, the authors reached a conclusion that instillation of mitomycin was superior

However, even when the pterygium was treated by the authors new method, the zero rate of recurrence was not attained 2-4 weeks after the operation, the state of limbus and the adjacent part was investigated in detail When the blood vessels show the tendency to invade the cornea, it is necessary to remove a small part adjacent to the limbus and to instill thio TEPA or mitomycin C after the removal for a week

In regard to the operation of the recurrent pterygium or the cases of post operative hard granulation, instillation after the operation is continued for a long while, or after a certain period, the instillation

Case 1

6 years old male (Fig 1) had right gradual proptosis of six months duration Proptosis increased on weeping The right eye showed a downward and inward severe proptosis of 30 mm Hertel (Left eye 15 mm) with limitation of ocular movements in all directions There were oedema of lids and chemosis of the conjunctiva A tense cyst was felt in the upper outer part of the orbit The cornea showed a corneal ulcer — due to lagophthalmos — preventing a clear view of the fundus Vision was 1/60

Under general anaesthesia and through a skin incision performed along the upper outer orbital margin a large, transparent tense cyst related to the orbital lobe of lacrimal gland, was seen extending backwards into the orbit The cyst ruptured during its blunt little finger dissection and about 15 cc clear watery fluid came out This was followed by spontaneous sliding of a mucoid cyst out of the wound Immediately the proptosis, oedema of lids, and chemosis of the conjunctiva disappeared The orbital part of the lacrimal gland was found firm lobulated greyish in colour A biopsy of the gland was taken

The mucoid cyst (Fig 2) was translucent 3 × 4 cm in size with a smooth surface and containing clear fluid On histopathological examination the cyst proved to consist of mucoid material The lacrimal gland tissue showed a mild chronic non specific interstitial inflammation (Fig 3)

(Fig 4) shows the child two weeks after the operation

Case 2

25 years old woman (Fig 5) complained of a painless gradually developing swelling of her right upper lid of seven months duration The right upper eyelid showed ptosis On elevating the upper lid a large tense smooth, transparent 3 × 2 cm cystic swelling which could be transilluminated was found projecting into the upper conjunctival cul de sac (Fig 6) The right eye was normal fundus normal vision 6/9

After an upper fornix conjunctival incision the cyst was easily separated from the surrounding tissues Histopathologically the cyst proved to consist of mucoid material being a mucoid cyst of Krause s gland duct Biopsy of the fornix subepithelial tissues surrounding the cyst showed a chronic non specific interstitial inflammation of Krause s glands (Fig 7) shows the patient one week after the cyst excision

In both cases the cyst was full of clear colourless thin watery fluid similar to tears The fluid was alkaline in reaction Cultures proved absence of organisms On microscopic examination the fluid contained only few degenerated epithelial cells The biochemical analysis of the fluid showed the presence of protein material sodium chloride urea sugar phosphates in the same percentage as in tears

Follow up of the two cases for two years showed absence of cyst recurrence

MUCOID CYSTS OF ORBITAL LOBE OF LACRIMAL GLAND AND OF KRAUSE'S GLAND

Report of Two Cases

ALY MORTADA, M.S.*

Cysts of the lacrimal gland are classified as retention cysts of the palpebral lobe "Dacryops", cysts of the orbital lobe, hydatid cysts and dermoid cysts. Although dacryops are relatively of frequent occurrence, cysts of the orbital lobe and cysts of Krause's glands especially cysts of mucoid nature were rarely reported in the literature.

Most cystic formations occurring in the orbital lobe are congenital in nature or neoplastic in origin (Duke Elder 1952). Retention cysts *of the orbital lobe were recorded by McMullen (1920) and Vrabec* (1918). Congenital cysts of the orbital lobe may appear clinically immediately on birth or be delayed for some years (Van Duyse and Van Lint 1922, Wood 1930 and others). Schornstein (1936) described such a congenital cyst showing highly vascularized tissue wall rich in *capillary network and multilayered epithelium.*

Cysts of Krause's glands are rare and usually occur as retention cysts in cicatricial conditions of the conjunctiva such as trachoma, or pemphigus (Stower 1892, Thompson and Chatterton 1905, Contino 1906, Ciocci 1932 and others) or after scar caused by excision of chalazion (*Paton 1919*). Giri (*1936*) and *Butler (1907)* reported cases where in no conjunctival scarring was evident.

Case Reports

In the two cases of mucoid lacrimal glands cysts to be described the general condition of the patients was good. Family history was of no importance. There was no history of trauma. There was no septic foci in the body or any genito urinary gonorrhoeal infection. Blood total and differential counts were normal. Blood Wasserman reaction, Casoni's test for hydatid cysts and tuberculin test were negative. Faeces were free of parasites and urine was free of albumin and sugar. X ray of both orbits, nasal sinuses and chest revealed normal findings. The left eye *in both cases was normal with normal fundus and vision 6/9.*

Right and left eyes in both cases showed palpebral and fornix conjunctival trachomatous scarring. Conjunctival smears and cultures were negative for organisms. There was no chronic dacryocystitis.

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CASE 2

FIG 5 Mucoid cyst of right upper Krause s glands in a woman aged 25 years Note swelling of upper lid and ptosis



FIG 6 Translucent large mucoid cyst of Krause s glands Upper lid is elevated to expose the cyst



FIG 7 Patient two weeks after removal of mucoid cyst of Krause s glands

DISCUSSION

In dacryops the lining of the cyst may resemble that of the ductule being composed of double layer of epithelium (Wiedersheim 1928 and others) in others there is a single layer of cylindrical epithelium (Gorlitz 1917 and others) in others the second layer is flattened endotheloid like cells (Goldzieher 1905 and others) or in others again goblet mucous cells are evident (Toth 1944 and others), while occasionally there are several layers of cells or profuse epithelial proliferation (Weekers 1909 and others) Probably many of these cases were conjunctival cysts present in the upper outer conjunctival fornix as in many of them goblet cells were present among the cyst epithelial lining and in others several layers of epithelium were present.

In the two described cases the presence of conjunctival trachomatous scars throws a light on the cause of the low grade chronic interstitial inflammation of the lacrimal gland or Krause s glands and the

CASE 1



FIG 1 Mucoid cyst of orbital lobe of right lacrimal gland in a male child aged six years Note severe proptosis

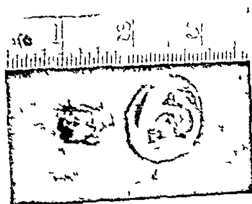


FIG 2 To the left is the large translucent mucoid cyst of orbital lobe of lacrimal gland To the right a piece of lacrimal gland removed for biopsy Note graduations in inches

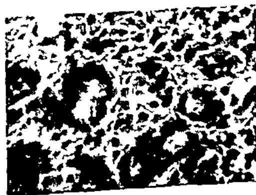


FIG 3 Orbital lobe of lacrimal gland showing chronic non specific interstitial inflammation (× 540)



FIG 4 The child two weeks after excision of the mucoid cyst of the orbital lobe of lacrimal gland Notice absence of proptosis

AMYLOIDOSIS OF THE CONJUNCTIVA WITH REVIEW OF 21 CASES

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Amyloid disease of the conjunctiva and eyelid is a rare but well authenticated entity It was first described by Von Oettingenr (1871) and then investigated in Russia by Raehlmann (1881) Kubli (1881) and Vossius (1889) Reports in the English literature are few in number Brief mention of the disease has been made by Fuchs (1919), de Schweinitz (1921), Collins and Mayo (1925) Wolff (1934), Berens (1936), Duke Elder (1938), Wiener (1946) and Castroviejo (1946) Ellis (1915) reported amyloid disease of the conjunctiva in a 30 year old woman who had mild conjunctivitis of the right eye for 2 years and hard induration of the lower lid for 3 4 months Guerry and Wiesinger (1960) have reported a case of primary amyloidosis of the eyelids and conjunctiva in a woman of 62 years of unknown aetiology

Amongst Indian observers cases have been reported by Reddi (1948), Srinavasan (1949) Wahi and Wahi (1954), Srivastava and Agrawal (1958) Mathur and Mathur (1959) and Ishwar Chandra and Sharma (1960) and recently by Darbari and Sehgal (1962)

CLASSIFICATION AND AETIOLOGY

Primary systemic amyloidosis is a rare disease of unknown cause Out of all the cases reported very few showed an involvement of the conjunctiva Reimann et al (1935) have recognised four varieties of amyloidosis (1) Primary (2) Secondary, (3) Localised amyloid tumour and (4) Amyloidosis associated with multiple myelomata Of these secondary amyloidosis is the most common form and is associated with long continued infective tissue destructive processes such as tuberculosis leprosy and osteomyelitis etc The organs most often involved are spleen kidneys liver and adrenals Primary amyloidosis which occurs in the absence of any known predisposing disease tends to involve the mesodermal tissues such as smooth and skeletal muscles cardiovascular system and skin

Most authorities have now accepted the contention that primary and secondary amyloidosis are closely related No clear cut distinction can be made between the two on the grounds of (1) Morphology of deposits including the staining characters (2) Distribution of deposits (3) Pathogenesis and (4) Chemistry According to Symmers (1956)

cause of mucoid degeneration of affected lacrimal or Krause's glands duct epithelial lining Also the trachomatous conjunctival scars are the cause of obstruction of the degenerated duct which distends by retention of tears giving the described clinical picture of mucoid cyst of orbital lobe of lacrimal gland or of Krause's glands

The three theories put for the formation of lacrimal gland cysts explain the formation of such mucoid cysts the presence of mild chronic inflammatory process around the ductules (Sourdille 1899), the presence of mucoid degeneration of duct epithelium (Goldzieher 1905) and the obstruction and dilatation of the excretory duct blocked by inflammatory influences (Lange 1899)

SUMMARY

1 Mucoid cysts of orbital lobe of lacrimal gland and of Krause s glands were rarely recorded in the literature The two reported cases represent the largest cyst of this kind and the first to be described from Egypt

2 In the two described cases mucoid degeneration of the affected lacrimal ductule was due to chronic dacryoadenitis probably of trachomatous origin Obstruction and thus distension of the mucoid cyst with tears were due to trachomatous conjunctival scarring

3 Mucoid cysts of the lacrimal gland or Krause s glands are loosely attached to their surrounding tissues and are thus easily removed

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EXPERIMENTAL ASPECTS OF EALES S DISEASE

By RYUTARO HAGINO

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In spite of the fact that 80 years have passed since the first description of Eales s disease by Henry Eales the etiology, methods of treatment and prophylaxis related to it have not yet sufficiently elucidated It is not even certain as to what the complete definition of this disease is Consequently it may be supposed that etiology of this disease is not easily defined by the experimental methods heretofore studied using of clinical cases

CLINICAL ASPECTS

In the present studies statistical analysis were carried out in 133 cases of recurrent intraocular hemorrhage in which definitely diag nosed systematic diseases were not included The age of the patients was generally young covering from 15 to 58 but most fell in the younger category of 15 to 35 (Table I) Out of 133 cases 103 were male and 30 female The right eye was affected in 51, left eye in 46 and both in 36 eyes

The important diseases in the patients past histories include lung tuberculosis rheumatism constipation, epistaxis, icterus kidney disease gastroptosis anal fistula hookworm disease anaemia tonsilitis and so on As eye complications uveitis, iridocyclitis, cataract and glaucoma were observed The skin tuberculin test was positive in 40 and negative in 9 of the 51 patients which showed accurate clinical history in the card and 21 patients out of 133 had long tuberculosis in their past histories (Table 2)

Besides these 133 patients the author observed a few cases who had clinical entity like Eales s disease and had both primary retinal and retino vitreous hemorrhage in old age That is uncertain whether or not these cases should be classified as Eales s disease or whether there must be further elucidation

Also from the standpoint of classification it may be supposed that some cases might develop from different cause e g previous case Buerger s disease sepsis and anaemia even though tuberculous symptoms existed were proved in the greater number of cases Conse quently in the studies of Eales s disease a more thorough examination of the etiology is first problem to be solved and clinical explanation especially problems of the treatment may be of secondary consideration

of hypertrophy of the tarsal plate and the conjunctiva were subjected to histopathological examination the number of such cases would be much greater Our 21 cases can be reviewed as follows —

Male = 15 cases
Female = 6 ,,

Age Incidence

10–20 years = 5 cases
21–30 ,, = 10 ,,
31–40 ,, = 4 ,,
Over 41 ,, = 2 ,,

It is obvious that it is more common in males and in the age period between 21–30 years On the other hand trachoma is more active in the younger age period i e between 1 and 6 years One may conclude that it is not the activity but rather the chronicity and repeated irritation that predispose the lids to such amyloid deposits and tumour formation One of these cases had chronic dacryocystitis as well and it was this eye which developed amyloidosis Like pterygia it is more common in males as they are constantly exposed to repeated irritations

Unilateral = 15 cases
Both lids = 8
One lid = 8
Bulbar conjunctiva also affected = 6 cases
In one case all the four eyelids were affected

CLINICAL APPEARANCE

The patients were quite healthy unlike cases of amyloid disease of kidneys or intestines The upper lid was affected more commonly (Fig 1) leading to tumour formation with mechanical ptosis and



Fig 1 Amyloidosis affecting the upper lid

the only criterion for primary amyloidosis is the absence of a recognised predisposing cause

Localised amyloidosis forming a small tumour like growth has been described in many sites including the respiratory tract, tongue, pharynx, thyroid, etc , but the aetiology of such amyloid deposits in the ocular tissues particularly in the lids is obscure Reddi (1948) Srinivasan (1949), Mathur and Mathur (1959), Ishwar Chandra and Sharma (1960) all think that it is secondary to trachoma or some other chronic irritation like dacryocystitis or chronic conjunctivitis Wahi and Wahi (1954) could not suggest an aetiologic agent in their own case Ellis (1915) in her report suggested nutritional deficiency as a possible aetiologic factor and Ashton described amyloid degeneration as a subgroup of hyaline infiltration of the eyelids In this respect he agreed with Duke Elder and Schmiedeberg (1920) who consider hyaline as a transitional product in the formation of amyloid from albumin Boyd (1960) thinks that all varieties of amyloidosis are probably related to one fundamental disturbance, the nature of which is still obscure It is also surmised that it may be a manifestation of hypersensitivity in which antibody is precipitated with polysaccharides of the ground substance Similarly Gilkes suggests that hyaline and amyloid degeneration of the conjunctiva may be regarded as variations of a single process where hyaline material is formed in the tissues as the result of a perversion of local protein metabolism Its extent to which this takes place will govern whether the appearances formed be those of hyaline or amyloid material

The aetiology of the disease is obscure in some cases as it is seen in normal individuals and clinically healthy eyes while in others it is secondary to some chronic irritative focus As the incidence of amyloidosis is greater in countries where trachoma is highly prevalent and that part of the conjunctiva most affected by the trachoma virus is more frequently involved, it appears that it bears a definite relationship to trachoma particularly in cases with a prolonged second stage Pathological examination of our cases also suggests this fact It also appears that conjunctival amyloidosis may not be so infrequent as is suggested in the literature

REVIEW OF 21 CASES

We have come across in our records of the past 7½ years, 21 cases which were admitted, investigated and operated upon in our hospital This is actually an underestimation of its incidence as some of the cases refused operation while in others the diagnosis was so obvious that the tissues were not sent for histological examination Three cases diagnosed by the pathologist as plasmocytoma are not included though they can also be grouped because they also stained metachromatically with methyl violet The incidence of trachoma in northern part of India varies from 54 per cent in the plains to over 80 per cent of population in the hill areas It is, therefore to be expected that amyloidosis would be more prevalent here We also feel sure that if all the cases

of hypertrophy of the tarsal plate and the conjunctiva were subjected to histopathological examination the number of such cases would be much greater Our 21 cases can be reviewed as follows —

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One of our cases was especially interesting since he gave a history of recurrent conjunctivitis the last attack lasting for nearly six months and he showed a papillary hypertrophic form of trachoma, stage II (M Callan s) The conjunctiva usually presents a half cooked potato appearance This appearance can be well appreciated during operation



FIG 5 (M P) Amyloidosis with calcification The section shows fibro collagenous stroma of tarsus containing large number of hyaline pink staining masses (amyloid material by special staining) some of which show calcium deposits Stroma shows intense collection of chronic inflammatory cells mag 21x



FIG 6 The same case under high power 60x Hyaline amyloid material is well seen



FIG 7 (M I) Amyloidosis with chronic inflammatory cells 60x Shows that tarsal tissue has almost completely undergone amyloid change containing a few hyaline concretions Stray cross collagen fibres are seen in stroma which contains chronic inflammatory cells especially plasma cells



FIG 8 (M) Amyloidosis post trachomatous 21x The section shows extensive amyloid change in the tarsal tissue including changes in the blood vessels There is tendency towards formation of pseudo-glands probably due to proliferation of the lining epithelium There is chronic inflammatory reaction and a degenerated lymphoid follicle under the epithelium

narrowing of the palpebral fissure (Fig 4b) *In some cases it was difficult even to evert the upper lid* The cornea was usually normal or showed ghost vessels of old trachoma Later on bulbar conjunctiva, caruncle and semilunar folds also became affected (Fig 2) In four of the early cases no mention is made about trachoma in the records



Fig 2 Amyloidosis affecting the lower lid with involvement of the bulbar conjunctiva



Fig 3 Amyloidosis affecting both the lids



Fig 4a Amyloidosis affecting the upper lid of the right eye



Fig 4b Amyloidosis affecting the upper lid of the right eye with narrowing of the palpebral fissure

HISTOLOGICAL EXAMINATION

All the cases were confirmed by histological examination In some cases the lid structure with its epithelium and follicles etc could be recognised while in other cases the whole tissue had undergone massive amyloid change In the fibrous stroma there could be seen a few criss cross collagen fibres and a few chronic inflammatory cells that is lymphocytes, plasma cells (5 cases) and occasional foreign body giant cell (3 cases) Special staining for amyloid material (Iodine and Congo red etc) was done in most of the cases The blood vessels particularly arteries, showed amyloid infiltration with end arteritis and thickened media In some cases mucous glands dilated with calcified concretions were seen Evidence of scarring and degenerated lymphoid follicles under the epithelium pointed out to the fact that they were post trachomatous Histological reports of six cases were as follows —

Case No 2 — R L 22 years Hindu female

Section showed irregular pieces of tissue These pieces consisted of irregular pink staining hyaline material (staining positive for amyloid) in which occasional stray spindle shaped cells were seen at the periphery A few lymphocytes and plasma cells were scattered throughout the tissue No stratified squamous epithelium or other epithelial structures of the lid were seen

Diagnosis Amyloid Disease of Lid

Case No 5 — S S 32 years Sikh male

Both the sections presented similar appearances They showed masses of hyaline pink staining material with focal collections of chronic inflammatory cells and a few blood vessels At places these cell collections enclosed a few foreign body giant cells Special staining was positive for amyloid material

Diagnosis Amyloid Deposit Eyelid

Case No 9 — S R 29 years Hindu male

All the biopsy pieces were covered superficially by squamous epithelium of the conjunctiva In the sub epithelial region there were hyaline pink masses which were structureless A few connective tissue strands fine blood vessels and collections of plasma cells were interspersed in between them The walls of the vessels were impregnated with similar material This material stained positively for amyloid substance

Case No 10 — M P 20 years Hindu male

The section showed fibro-collagenous stroma of the tarsus containing a large number of hyaline pink staining masses which were

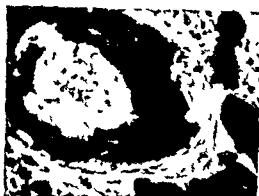


Fig 9 *The same under high power 140x*



Fig 10 (*J*) *Amyloidosis post trachomatous 60x The section is lined by squamous epithelium The sub-epithelial tissue shows infiltration with chronic inflammatory cells and the rest shows deposit of amyloid material This area is also rich in blood vessels probably indicating that amyloid degeneration has occurred after granulomatous reaction in the tissue*



Fig 11 (*A R*) The section (Mag 60x) shows amyloid degeneration in tarsal plate forming homogeneous eosinophilic masses The blood vessels do not show much amyloid changes The infiltration with cells is also scanty (Primary amyloidosis)

and is diagnostic and typical In other cases definite trachomatous scarring was encountered

Out of our eight recent cases four of them confirmed and admitted that they had also passed through the same second stage for a long period before treatment was sought So we suggest that those patients of trachoma who suffer from a prolonged second stage are more predisposed to amyloidosis than others

Laboratory investigations were not of much help Differential and total W B C counts, W R , Kahn test, urine, stools, conjunctival smear tests contributed little Blood cholesterol values were estimated in only 7 cases and were within normal limits The liver, spleen kidneys and cardiovascular system were normal in all cases

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Case No 10 — M P 20 years Hindu male

The section showed fibro collagenous stroma of the tarsus con taining a large number of hyaline pink staining masses which were

irregularly distributed A number of these masses showed deposits of calcium No bony trabeculae were discernible The stroma showed intense collection of chronic inflammatory cells Special staining showed the hyaline masses to be amyloid (Figs 5 and 6)

Diagnosis Amyloid Tumour of the Lid

Case No 13 — J, 14 years, Hindu male

The tissue was covered by squamous epithelium The subepithelial tissue was infiltrated with chronic inflammatory cells and beneath the epithelium there was a deposit of amyloid material This area was also rich in blood vessels, thereby indicating amyloid degeneration following granulomatous reaction in the tissue (Fig 10)

Diagnosis Amyloidosis—Post Trachomatous

Case No 14 — M A, 38 years, Mohamedan male

MUSHTAQ AHMAD 38 MOHAMEDAN MALE

The section showed that the tissue had undergone amyloid change for the most part Hyaline concretions were also seen There were stray collections of chronic inflammatory cells, specially the plasma cells Von Gieson stain showed a few criss cross collagen fibres, while the rest had undergone amyloid degeneration Methyl violet stain showed metachromasia of the homogeneous amyloid mass (Fig 7)

Anatomical Diagnosis Amyloidosis—Post Trachomatous

Case No 15 — I R, 42 years, Mohamedan male

The section showed the tarsal plate to be most affected by amyloid degeneration in the form of homogeneous eosinophilic masses while this change was not prominent in the blood vessels The amyloid material had taken a bright khaki stain with Von Gieson and showed metachromasia with Methyl violet stain (Fig 11)

Anatomical Diagnosis Amyloidosis—Primary

Case No 16 — M, 22 years Hindu male

The section showed that the tissue for the most part had undergone amyloid changes The blood vessels also showed amyloid degeneration There was little normal glandular tissue remaining probably as a result of the proliferation of the lining epithelium to form pseudoglands There was infilteration with chronic inflammatory cells and at one place a degenerated lymphoid follicle under the epithelium (Figs 8 and 9)

Anatomical Diagnosis Amyloidosis—Post Trachomatous

TREATMENT

The growth should be removed together with the tarsal conjunctiva and tarsal plate leaving only 1 to 2 mm near the lid margin

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(Tarsectomy) The remaining tarsal plate is then sutured to the conjunctiva and levator muscle near the fornix by three double armed sutures (Modified Blascovics operation) If the bulbar conjunctiva is involved it has to be slowly dissected and shelled out as the growth is subconjunctival The raw areas can be repaired by mucus membrane grafts from the lip The pieces of friable tissues should be carefully removed because if some portions are left they have tendency to redevelop as occurred in three of our cases, one of which had been operated upon about ten years previously Recurrences have been reported by Duggan and Chitnuts (1950) hence post operative radio therapy is further suggested (Redi 1949) We have tried Beta therapy 6000-9000 rep by strontium 90 applicator

SUMMARY

Amyloidosis of the conjunctiva is more common than generally suggested It may be primary but most of the cases occur in areas where trachoma is predominant and are secondary to the chronic irritation which is a sequel to this disease It is suggested that those cases which have a prolonged untreated second stage of the papillary hypertrophy type are probably more predisposed to amyloidosis 21 investigated cases found in our records of the past 7½ years are reviewed As after excision the possibility of a recurrence cannot be ruled out it is further suggested to give beta therapy in such cases

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OPERATIVE TREATMENT OF XEROPHTHALMIA BY TRANSPLANTATION OF DUCTUS STENONI INTO CONJUNCTIVAL SAC

Professor A B KATSNELSON and master of medical science
P S KAPLOONOVICH
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For many centuries physicians had no means to provide permanent moistening of the xerophthalmic eye and the patients with xerophthalmia were condemned to agonizing blindness

In 1951 the author proposed a surgical method of treatment of xerophthalmia which consists in displacement of ductus Stenoni *into the conjunctival sac* The approach to the sac is effected by a cut through skin In the same year Filatov and Shevelev independently of the author also proposed the transplantation of ductus Stenoni separating the latter in the substance of the cheek through a cut in the mucous membrane of the mouth For the past eleven years the operation done mostly by our method received a wide support On the subject there was much written in the Soviet and foreign press

In the process of elaborating the method we have introduced different modifications that have simplified the technique of operation which considerably increased number of persons who could undergo it

Our research made on healthy persons by means of contrast X ray of ductus Stenoni (sialography), showed that the duct is long enough to be displaced into the conjunctival sac only in half of the cases We have in mind here not so much the absolute length of the duct as the length useful in the transplantation that is the linear distance from the outlet of the duct at the gland to the corner of the eye Thus simple computation should be made before the operation (2) (2a) When preliminary sialography shows absolute or relative insufficiency of the duct we lengthen the latter to the necessary size by means of a tube formed from the mucous membrane of the cheek (3)

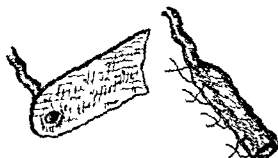
The operation itself consists in a skin cut corresponding to the duct projection 1) its delicate separation together with an area of mucous membrane (round or square) surrounding the orifice of the duct(4) Form and size of the resected mucous membrane depend on the necessary lengthening of the duct If there are additional branches of the duct they are severed and tied To make the final separation of the duct easier we introduced two instruments One is a round or a rectangular protruser that is put on the duct it pushes the mucous membrane of the mouth out and the other is a large diameter trephine that easily resects the mucous membrane. (5 6)



2 Contrast X Ray photo of the *ductus stenoni*



2a A Diagram of computation of the duct length necessary *for its displacement* to the eyeball



3 Lengthening of the duct

Lengthening of the duct

After the separation of the duct the hole in the mouth is sutured (8) Then four holder stitches are applied to the resected mucous membrane surrounding the orifice of the duct (7) From the *operation wound* in the cheek an *underskin tunnel* opening into the *conjunctival sac* at the outer corner is made with a wide *flat knife* The holder stitches are then taken by long thin pincers that are passed through the tunnel (9) and the stitches are pulled through it to be sewn to the conjunctiva of the lower fornix If the conjunctival sac is insufficient it can be increased by the *mucous graft from the mouth* To *prohibit infection* the cheek is infiltrated with a solution of antibiotics

Up to now we have performed thirty three operations on the eyes of patients with severe xerophthalmia A positive result was



Fig 7 Ductus Stenoni has been freed with the surrounding mucous of the cheek.



Fig 1 A patient before operation A line of dissection is marked according to sialography findings



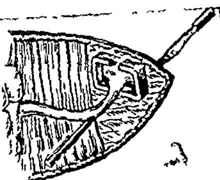
Fig 8 A hole in the mucous of the cheek after separation of the duct



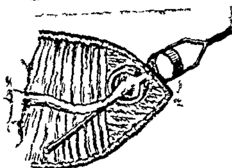
Fig 4 The duct bluntly separated from the surrounding tissues. A rubber strip is placed under it



Fig 9 Forming of the underground tunnel and stretching of the duct to the eye by holder stitches.



5 A Rectangular Protruser at work (a diagram)



6 Round protruser and knife at work (a diagram

obtained in thirty cases The most frequent complications encountered by us were infection (three cases) downward displacement of the duct (two cases) and temporary ceasing of gland function probably due to trauma of nerve fibres When the duct slips out of the conjunctival fornix a cut in skin is made at the lower margin of the orbit and the duct stitched again

We have satisfied ourselves that serous saliva offers excellent tear substituting fluid This can be explained by its great chemical and physical closeness to the tears The eye excellently stands the operation Xerotic patches usually disappear or diminish in the very first few days Also there is a large decrease in the number of keratic cells in the scrapings of the conjunctiva In some cases separate dry areas persist This can be ascribed to great trophic changes in the basal epithelium The patients cease to feel the tormenting dryness In most cases the acuity of vision is increased The moistened eyes can undergo optical operations (transplantation of cornea iridectomy etc) well

The only defect of the new operation is the flow of saliva during taking of food There were several methods *proposed for* elimination of the excessive salivation severing of nervi auricule temporalis, conjunctiva antrostomy (Bennet) partial resection of parotid gland We have successfully irradiated parotid gland (single dose of 120r to 150r Total dose being 600r to 1500r controlling the therapeutic effect by Schirmer s test)

ETIOLOGICAL PROBLEMS IN UVEITIS

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Universitäts Augenklinik, *Zurich*

Every ophthalmologist is able to settle the diagnosis of uveitis on the spot and he usually starts treating it immediately But in most cases this treatment will be purely symptomatic

We usually assume that uveitis is an inflammatory disease and at the same time we think of a reaction between some unknown antigen and a specific antibody This reaction sets free histamin like products causing inflammation Antiallergic drugs and steroids will certainly influence this reaction but will never reveal the etiology

Many attempts have been undertaken to demonstrate specific antigen in the diseased eye, be it bacterial, viral or a parasitic Positive results for about every possible infective agent have been reported in the literature, but mainly on enucleated eyes These findings are very important for our knowledge of endogenous eye diseases, but this kind of investigation did never have much clinical value The percentage of positive results is much too low, most cases remain unsolved problems

We have therefore paid more attention to the detection of specific antibodies in the eye It must be said that despite the great work of *A C Woods* there is no reason to believe that a specific infection in the eye leads to an increase of specific antibodies in the blood or to an increased sensitivity of the skin Very recent studies of *Hallett, Wolkowicz, Feria, Leopold and Wyzenski* and also of *Coles* have shown, that blood tests alone (Middlebrook Dubos Test for Tbc, Antistrepto lysine O Test) are of no value in the diagnosis of uveitis cases It is therefore very strange that everybody still believes very much in the diagnostical value of the Dye test (Sabin Feldmann) for the detection of toxoplasmosis One should be aware that all these tests be it blood tests or skin tests can only be conclusive if they are negative Then at least we know, that this kind of infection is very unlikely to be the cause of an eye infection

We can assume that for practical purposes, a local antigen antibody reaction within the eye leads to a surplus of antibody This antibody will most certainly remain fixed within the tissue But part of it will leak into the blood stream, and part of it may get into the intraocular fluids (vitreous, aqueous humour) If we can determine these antibodies quantitatively within the blood, and at the same

EXPERIMENTAL ASPECTS OF EALES S DISEASE

By RYUTARO HAGINO

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Nagoya City University Medical School,
Nagoya Japan

In spite of the fact that 80 years have passed since the first description of Eales s disease by Henry Eales the etiology, methods of treatment and prophylaxis related to it have not yet sufficiently elucidated It is not even certain as to what the complete definition of this disease is Consequently it may be supposed that etiology of this disease is not easily defined by the experimental methods heretofore studied using of clinical cases

CLINICAL ASPECTS

In the present studies statistical analysis were carried out in 133 cases of recurrent intraocular hemorrhage in which definitely diag nosed systematic diseases were not included The age of the patients was generally young covering from 15 to 58 but most fell in the younger category of 15 to 35 (Table 1) Out of 133 cases, 103 were male and 30 female The right eye was affected in 51 left eye in 46 and both in 36 eyes

The important diseases in the patients past histories include lung tuberculosis rheumatism constipation epistaxis, icterus kidney disease gastroptosis anal fistula hookworm disease anaemia, tonsilitis and so on As eye complications uveitis iridocyclitis, cataract and glaucoma were observed The skin tuberculin test was positive in 40 and negative in 9 of the 51 patients which showed accurate clinical history in the card and 21 patients out of 133 had long tuberculosis in their past histories (Table 2)

Besides these 133 patients the author observed a few cases who had clinical entity like Eales s disease and had both primary retinal and retino vitreous hemorrhage in old age That is uncertain whether or not these cases should be classified as Eales s disease or whether there must be further elucidation

Also from the standpoint of classification it may be supposed that some cases might develop from different cause e g previous case, Buerger s disease sepsis and anaemia even though tuberculous symptoms existed were proved in the greater number of cases Conse quently in the studies of Eales s disease a more thorough examination of the etiology is first problem to be solved and clinical explanation, especially problems of the treatment may be of secondary consideration

TABLE 1 *Distribution of Age in 133 cases of Eales's disease*

Age	Male		Female		Total	
	No. of Cases	% of Cases	No. of Cases	% of Cases	No. of Cases	% of Cases
15~19	13	13.8	8	26.6	21	20.3
20~24	18	14.3	4	13.3	22	13.8
25~29	33	29.4	5	16.7	38	23.1
30~34	14	11.6	6	20.0	20	15.8
35~39	8	9.2	2	6.7	10	7.9
40~44	5	7.3	2	6.7	7	7.0
45~50	6	6.5	0	0.0	6	3.2
50~54	5	5.9	2	6.7	7	6.3
55→	1	2.0	1	3.3	2	2.6
Total	103	100.0	30	100.0	133	100.0

TABLE 2 *Tuberculin Test in 51 cases of Eales's disease*

	(−)	(±)	(+)	(++)	*Total*
Male	7	2	23	9	41
Female	2	0	7	1	10
Total	9	2	30	10	51

STUDIES ON CONSTITUTION OF THE BLOOD IN THE PATIENT OF EALES'S DISEASE

The experiments were carried out to study the portent of the change of blood of patients in the mechanism of hemorrhage.

Injection of patient serum into the vitreous body of the rabbit. Since Oguchi's first description many students have tried the same experiments to elucidate the onset of retinitis proliferans.

In the present studies autoblood was injected into vitreous of the same rabbit both in complete blood and separated components e.g. red blood cells, white blood cells, serum and hemoglobin.

The results obtained from this experiment duplicated the many changes as appeared in pre ious literatures, showing the dilatation of vessels, fibroblasts and sprouting capillaries which invadea the vitreous from the retina the changes of outer layer of the retina, and so on As the mo t marked change a substance like ceroid pigment was observed in Oil red 0 stained specimen

Fibrinolysin in the blood or in the vessel wall tissues The studies on fibrinolysin in the blood of Eales s disease are still unsettled In the present experiments the author su pected the existence of some relationships between the retinal hemorrhage and fibrinolysin in the blood or in the vessel wall tissues and from this standpoint proteinase capillary permeability promoting action and capillary resistance were measured

In the results obtained the above three factors proved markedly positive during a bleeding attack but all these phenomena do not always appear and neither they are characteristic of Eales s disease (Table 3)

With this experimental fact in mind serum was obtained during a retinal hemorrhage was experimentally injected into rabbit vitreous and that in turn caused retinal and vitreous hemorrhage

The results are very important because it shows presence of some substances in the serum which plays an important role in a retinal hemorrhage

STUDIES ON RETINAL AND VITREOUS HEMORRHAGE USING DEAD BCG VACCINES

As mentioned above the etiology of Eales s disease is not yet decided but a large number of the cases were elucidated as tuber culosis or tubercular allergy Many experimental studies were carried out to solve this question using live tubercle bacilli In the present studies the author tried to explain it by dead BCG vaccines

EXPERIMENTAL METHODS

Dead BCG vaccine was made by the following methods BCG vaccine was suspended into physiological solution of sodium chloride and killed by steamheating at 100 C for 30 minutes in Koch s steam sterilizer

The experimental methods were carried out as follows (1) Injection of dead BCG vaccines into the common carotid artery 2) *Injection* of the vaccines into the rabbit vitreous body (3) Injection of the vaccines into the carotid artery and at the same time into the vitreous (4) Injection of the vaccines into the auricular vein these *procedures* were carried out on sensitized and non sensitized rabbits

The results obtained In the non sensitized rabbits with dead BCG *vaccine injection into* carotid artery spotted hemorrhages in the peripheral retina were observed 3 days after injection Retinal vessels dilated a *little* and sometimes projected into the vitreous These

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30～34	14	11.6	6	20.0	20	15.8
35～39	8	9.2	2	6.7	10	7.9
40～44	5	7.3	2	6.7	7	7.0
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TABLE 3 *Fibrinolysin in the Blood in the patient of Eales s disease*

No of Cases	Age Sex	Diagnosis	Recurrents of Hemorrhage	Cr	F	CPP × 25	CPP × 50	CPP × 100	Note
1	33	Control		−	−	6 × 5	5 × 5	4 × 4	
2	25	Control		+	+	8 × 8	6 × 6	5 × 4	
3	26	Control		−	−	5 × 5	5 × 4	3 × 3	
4	23	R V H	3	−	+	9 × 8	6 × 6	5 × 5	
5	32	V O & H	1	±	++	8 × 8	8 × 7	6 × 6	
6	35	R V H	1	−	++	5 × 4	5 × 4	1 × 1	Plegnancy 8 Mon
7	40	R V H	1	±	+	8 × 8	6 × 5	4 × 3	5 Days before the Hemorrhage
8	20	R V H	2	+	++	11 × 9	8 × 7	8 × 6	In the Midst of H
			2	−	±	6 × 6	5 × 4	3 × 3	7 Days before the Hemorrhage
			3	+	++	6 × 6	4 × 4	3 × 3	In the Midst of H
			3	−	+	6 × 5	5 × 4	4 × 3	3 Days after the Hemorrhage
9	27	R V H	1	−	+	9 × 8	8 × 7	7 × 6	3 Days after the Hemorrhage
10	23	Periphlebitis		+	+++	9 × 8	8 × 7	6 × 6	Epistaxis
11	16	R V H	2	+	++	10 × 9	9 × 9	9 × 9	Epistaxis and Anal Bleeding 2 Days after this procedure

R V H Retinal and Vitreous Hemorrhage
V O & H Vitreous Opacity and Vitreous Hemorrhage
Cr Capillary Resistance F Fibrinolysin C P P Capillary Permeability Promoting Action

retinal changes by intravitreous injection were more marked than these of the former method

The following results were obtained in sensitized rabbits First sensitization method Dried BCG vaccine was suspended into physio logical solution of sodium chloride and inoculated intracutaneously

1st injection	0 25 mg/0 2 cc
2nd injection	0 5 mg/0 2 cc
3rd injection	0 75 mg/0 2 cc

In this experiment the hemorrhages on the papilla surface of the rabbit were seen 12 days after a carotid artery injection

Next pathological observations The changes of the retina retinal vessels choroid and vitreous body were observed respectively Especially hemorrhage lesions seen with the naked eye were caused by rupture of the retinal vessels or sprouting capillaries Moreover marked retinal changes and cell infiltration in choroidal tissues were observed (Fig 1)

When it was injected into auricular vein no retinal hemorrhage or other retinal changes were observed

The injection of dead BCG vaccines proved that peripheral hemorrhages vascular changes and proliferated changes of the retina were caused by that procedure on non sensitized rabbits (Fig 2) However in the sensitized animals retinal hemorrhages were observed at central area and on the surface of the papilla (Fig 3) The mecha nism of hemorrhage is supposed to have a relationship with rupture of the vessel walls or diapedesis

In intravenously injected cases vitreous body became cloudy on the day following injection so that the hemorrhage was visible in the retina but by the histo pathological study many other marked changes were revealed There were wandering cells proliferation of the tissues cell infiltration surrounding the vessels and sprouting capillaries (Fig 4 & 5)

From these results it is presumed that the hemorrhage and recurrent hemorrhage have some association with allergic or pre allergic state

EXPERIMENTAL STUDIES ON HEMORRHAGE OF THE RETINA AND VITREOUS BODY WITH HYDRODYNAMIC METHOD AND SNAKE VENOM

Mizuno et al studied on fragilities of retinal vascular *system* by hydrodynamic method and then by a vascular tree specimen by Hausler and Sibay s technique From this experiment it was revealed that arteries show no changes but vein of the retina is weaker than that of the brain (Fig 6)

Studies on hemorrhage with snake venom

To begin with a minimum dose inducing hemorrhage was measured and it was decided that density over 0 5/0 2 cc was necessary to bleed

TABLE 3 *Fibrinolysin in the Blood in the patient of Eales's disease*

No of Cases	Age Sex	Diagnosis	Recurrents of Hemorrhage	Cr	F	CPP			Note
						/ 25	⋎ 50	⋎ 100	
1	33	Control		−	−	6 / 5	5 × 5	4 × 4	
2	25	Control		+	+	8 × 8	6 × 6	5 × 4	
3	26	Control		−	−	5 × 5	5 / 4	3 / 3	
4	23	R V H	3	−	+	9 × 8	6 / 6	5 / 5	
5	32	V O & H	1	±	++	8 / 8	8 ⋎ 7	6 × 6	
6	35	R V H	1	−	++	5 ⋎ 4	5 × 4	1 × 1	Plegnancy 8 Mon
7	40	R V H	1	±	+	8 / 8	6 / 5	4 / 3	5 Days before the Hemorrhage
8	20	R V H	2	+	++	11 / 9	8 / 7	8 × 6	In the Midst of H
			2	−	±	6 ⋎ 6	5 ⋎ 4	3 ⋎ 3	7 Days before the Hemorrhage
			3	+	++	6 / 6	4 / 4	3 ⋎ 3	In the Midst of H
			3	−	+	6 ⋎ 5	5 ⋎ 4	4 × 3	3 Days after the Hemorrhage
9	27	R V H	1	−	+	9 / 8	8 ⋎ 7	7 × 6	3 Days after the Hemorrhage
10	23	Periphlebitis		+	+++	9 / 8	8 / 7	6 ⋎ 6	Epistaxis
11	16	R V H	2	+	++	10 ⋎ 9	9 / 9	9 / 9	Epistaxis and Anal Bleeding 2 Days after this procedure

R V H Retinal and Vitreous Hemorrhage
V O & H Vitreous Opacity and Vitreous Hemorrhage
Cr Capillary Resistance F Fibrinolysin C P P Capillary Permeability Promoting Action

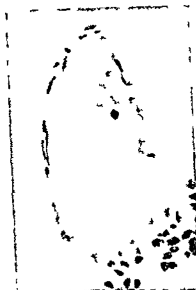


Fig 5 (Hagino and Tamura) Eosinophilic leukocytes in the blood of the retinal vein 3 days after the injection of dead BCG vaccines into the carotid artery (Non sensitized rabbit H E stain x 800) Same animal as in Figure 2



Fig 6 (Mizuno Miyata and Tamura) Dilating venula by the hydrodynamic method Equator area of the retinal vessels (Young cat vascular tree specimen x 60)



Fig 7 (Mizuno Miyata and Tamura) The disorganized reticular structure in the outside of the venula with the intravitreous injection of snake venom (Young cat vascular tree specimen x 600)

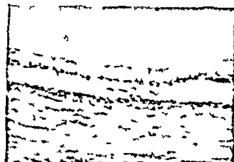


Fig 1 (Hagino and Tamura) The part of marked retinal changes and cell infiltration in choroidal tissues 12 days after the injection of dead BCG vaccines into the carotid artery (Sensitized rabbit H E stain x 200)

Fig 2 (Hagino and Tamura) Hemorrhages vascular changes and proliferated changes of the peripheral retina 3 days after the injection of dead BCG vaccines into the carotid artery (Non sensitized rabbit H E stain x 800)





Fig 3 (Hagino and Tamura) Hemorrhages on the surface of the papilla 12 days after the injection of dead BCG vaccines into the carotid artery (Sensitized rabbit H E stain x 280) *Same rabbit as in Figure 1*



Fig 4 (Hagino and Tamura) Hyalinosis of the part of the retinal vein (Non sensitized rabbit H E stain x 800) Same rabbit as in Figure 2

The results obtained In all cases just after injection the retina became anaemic, and the papilla pale In 5 20 minutes the blood current became visible while the arteries continued their contraction, and the veins dilated

After that various changes appeared *e g* luxation of lens cataract and glaucoma Next retinal haemorrhages began to appear on the surface of papilla or its surrounding area and gradually hemorrhages expanded to peripheral vessels especially to veins (Fig 9) The changes of the fundus differ from each other according to experimental condition of injected substances

Histo pathological findings Blood and wandering cells were observed on the surface of the papilla Besides the arteries swelled and were surrounded by eosinophil leucocytes, the vein dilated and became thinner

In peripheral retina there were haemorrhagic lesions caused by rupture of the vessels Generally retinal changes were more remark able in neuroepithelial layer but brain layer stayed almost intact In the changes noted after 15 days the papilla looked like choked disc

The clinical and pathological findings above noted were ob erved in the cases were injected 1000 u/0 1 cc solution of α chymotrypsin (Fig 10)

In the cases of 500 u/0 1 cc 6 hours after injection the vessels on the surface of papilla seemed to be in pre bleeding state and suffered from eosinophil leucocytes (Fig 11)

In the peripheral area of retinal haemorrhages were proved to exist which should have been caused by rupture of the vessel walls In this case also thrombus formation was observed (Fig 12)

In the case of 50 unit injection haemorrhages were also observed in peripheral area and also thrombus formation 15 days later haemorrhages disappeared spontaneously In the case in which 1 unit was injected only wandering of red blood cells was proved as changed condition after 15 hours

From the results noted above it was well clarified that for the studies of retinal haemorrhage adequate dose of α chymotrypsin should be from 10–15 u 0 1 cc Moreover it is notable phenomenon that retinal haemorrhage appears in nasal side and it recurs This problem is not yet elucidated

STUDIES ON RETINAL HAEMORRHAGE WITH ε AMINOCAPROIC ACID

Recently aminocaproic acid is used in order to stanch in clinic for the reason that this substance inhibits activation of enzyme However if ε aminocaproic acid is administrated continously fibri nolysin becomes voluminous or is activated against such substance The present studies were carried out to elucidate the relationship between a function of proteinase and its inhibitor

So 200, 50, 5, 0 5/0 2 cc snake venom solution were injected into rabbit vitreous body, respectively After injection retinal haemorrhaging began at different times according to density of venom In the beginning spotted haemorrhages appeared on the surface of papilla and its surroundings, and gradually increased Then the haemorrhages were *observed at peripheral vessels During 1 2 hours haemorrhagic area* expanded and at the same time more vitreous haemorrhages were observed

Histo pathological findings Generally venule is more invaded than arteriole In PAS staining of the arteriolar walls they are very similar to these of normal vessel, but venule walls stain unevenly Moreover nucleus shows caryolysis or nuclear swelling In some lesions, rupture of vessel *walls* and *haemorrhages* are revealed

In the next experiments 5 and 0 5/0 2 cc snake venom were injected into young cat vitreous Time duration of bleeding in cat is longer than that of rabbit Haemorrhages first appeared in spots at equatorial area and gradually increased in number and extended, resulting in vitreous bleeding Furthermore, those haemorrhages appear along the veins Vascular system surrounding the papilla shows no marked changes, but at peripheral area reticular structure present in the outside of vein is lost and shows homogenous structure and varicocele like structure Capillaries lost normal anastomosis, showed marked meandering and the wall became thinner (Fig 7)

Histo pathological findings Marked haemorrhages were seen between inner limiting membrane and ganglionic cell layer The wall of venule became remarkably thin Nucleus showed vacuolization and in some area no polysaccharide *staining was observed Moreover,* ganglionic cell layer was markedly destroyed (Fig 8)

The results obtained by injection of snake venom into carotid artery differed from these by the former method Particularly no changes were observed in veins

In previous experiments, the following facts were elucidated The tissue changes caused by venom attack from outside were more remarkable than these from inside of vessel wall Fragilities of venule and capillaries were caused only by invasion from outside

It is well known fact that the influences of snake *venom on the* vein wall should be caused mainly by activity of proteinase In the *present* experiment it was suspected that the retinal vein was affected more easily from outside

STUDIES ON RETINAL HEMORRHAGE WITH *α* CHYMOTRYPSIN

Experimental methods α chymotrypsin solution of 1000 u/0 1 cc 500 u/0 1 cc, 5 u/0 1 cc, 1 u/0 1 cc respectively was injected into rabbit vitreous body Observation was carried out in two groups one from 6-15 hours after injection, and the other from 15 25 days after

The results obtained In all cases just after injection the retina became anaemic, and the papilla pale In 5 20 minutes the blood current became visible while the arteries continued their contraction, and the veins dilated

After that various changes appeared *e g* luxation of lens, cataract and glaucoma Next retinal haemorrhages began to appear on the surface of papilla or its surrounding area and gradually hemorrhages expanded to peripheral vessels especially to veins (Fig 9) The changes of the fundus differ from each other according to experimental condition of injected substances

Histo pathological findings Blood and wandering cells were observed on the surface of the papilla Besides, the arteries swelled and were surrounded by eosinophil leucocytes the vein dilated and became thinner

In peripheral retina there were haemorrhagic lesions caused by rupture of the ves els Generally retinal changes were more remark able in neuroepithelial layer but brain layer stayed almost intact In the changes noted after 15 days the papilla looked like choked disc

The clinical and pathological findings above noted were observed in the cases were injected 1000 u/0 1 cc solution of α chymotrypsin (Fig 10)

In the cases of 500 u/0 1 cc 6 hours after injection the vessels on the surface of papilla seemed to be in pre bleeding state and suffered from eosinophil leucocytes (Fig 11)

In the peripheral area of retinal haemorrhages were proved to exist which should have been caused by rupture of the vessel walls In this case al o thrombus formation was observed (Fig 12)

In the case of 50 unit injection haemorrhages were also observed in peripheral area and also thrombus formation 15 days later haemorrhages disappeared spontaneously In the case in which 1 unit was injected only wandering of red blood cells was proved as changed condition after 15 hours

From the results noted above it was well clarified that for the studies of retinal haemorrhage adequate dose of α chymotryp in should be from 10-15 u 0 1 cc Moreover it is notable phenomenon that retinal haemorrhage appears in nasal side and it recurs This problem is not yet elucidated

STUDIES ON RETINAL HAEMORRHAGE WITH α AMINOCAPROIC ACID

Recently ε aminocaproic acid is used in order to stanch in clinic for the reason that this substance inhibits activation of enzyme However if ε aminocaproic acid is administrated continously, fibri nolysin becomes voluminous or is activated against such substance The present studies were carried out to elucidate the relationship between a function of proteinase and its inhibitor



Fig 8 (Mizuno Miyata and Tamura) Retinal haemorrhages with the intra vitreous injection of snake venom (Young cat H E stain, × 280)

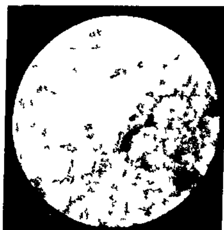


Fig 9 (Hagino and Tamura) Fundus photograph of the retinal haemorrhage in the peripheral areas 3 days after the intravitreous injection of α chymo trypsin (50 u/0 1 cc) (Colored rabbit)



Fig 10 (Hagino and Tamura) Retinal haemorrhage on the surface of the papilla or its surrounding area and marked changes of the vessels 6 hrs after the intravitreous injection of α chymotrypsin (1000 u/0 1 cc) (Colored rabbit H E stain × 600)



Fig 11 (Hagino and Tamura) Pre bleeding state with eosinophilic leuko cytes infiltration 6 hrs after the intravitreous injection of α chymo trypsin (500 u/0 1 cc) (Colored rabbit H E stain × 200)



FIG 12 (Hagino and Tamura) Haemorrhages and thrombus formation of the retinal vessels 3 days after the intravitreous injection of α-chymotrypsin(500 u 0 1 cc) (Colored rabbit H E stain x 1500)

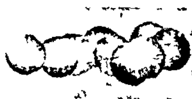


FIG 13 (Hagino and Tamura) Fundus photograph of retinal haemorrhage in the peripheral areas 2 days after the intravitreous injection of ε aminocaproic acid (0 02 g 0 1 cc) (Albino rabbit)

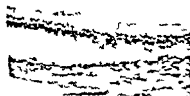


FIG 14 (Hagino and Tamura) Haemorrhage in the peripheral retina 2 days after the intravitreous injection of ε aminocaproic acid (0 02 g/0 1 cc) (Albino rabbit H E stain x 280)

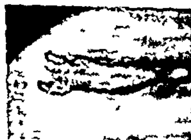


FIG 15 (Hagino and Tamura) Vascular tree of the haemorrhage in the retinal capillaries 2 days after the intravitreous injection of ε-aminocaproic acid Same rabbit as in Figure 13

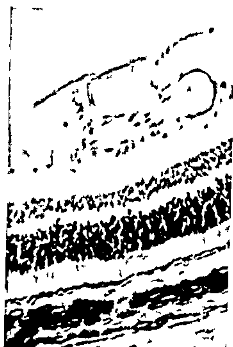


Fig 8 (Mizuno Miyata and Tamura) Retinal haemorrhages with the intravitreous injection of snake venom (Young cat H E stain x 280)



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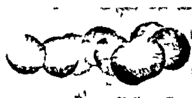


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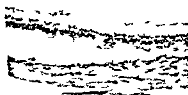


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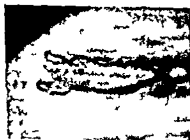


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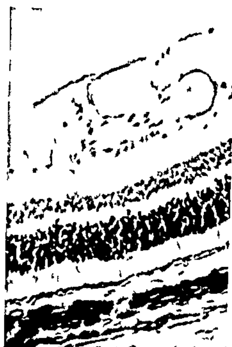


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Experimental methods 0 02g/0 1 cc *solution of* ε aminocaproic acid was injected into vitreous body of the rabbit *3* days later China ink was injected into the auricular vein of the same rabbit

Just after injection slight dilatation of retinal vein was *observed* 2 days later capillary haemorrhages of the retina appeared (Fig 13) 3 days *later* extended specimen of the retina was made from the rabbit *injected 10 cc China ink By* studies on this vascular tree specimen spot shaped haemorrhages of the retina were noticed (Fig 14, 15)

Of the results obtained it may be supposed that activation of proteinase also is induced by injection of enzyme *inhibitor*

COMMENT AND SUMMARY

Nowadays the etiology of Eales's disease is still not defined clearly, and at the same time it is neither clear that what clinical findings are included in this disease Consequently, experimental studies on this disease revealed various difficulties to settle experimental signs Actually the studies are not rare, but most of them are limited to clinical field

In the present studies the mechanism of retinal and vitretous haemorrhages was selected as the first thing to be solved To attain this object the studies on the characteristic blood structure of the patient, structure of retinal vessel walls and studies on influences of various enzymes on the vessel were carried out using different experimental methods From these experiments a number of suspected problems could have been solved

During the retinal haemorrhage, fibrinolysin in the blood is activated, and at the same time capillary permeability promoting action becomes stronger On the other hand, retinal hemorrhage by the intravitreous injection of patient's serum of Eales's disease has been detected Other experiments were tried to clarify the meaning of the walls of the retinal vessel on haemorrhage For this purpose the experiments noted above were carried out using snake venom, α chymotrypsin Or ε aminocaproic acid

The results obtained show that there is a definite relationship between activation of proteinase in the walls of retinal vessel and retinal haemorrhages As it is well known, blood pressure of the retinal capillary is high and moreover, resistance in the walls of the retinal veins is weaker than that in the brain Accordingly, when the walls were influenced from some disease, for example from tuberculosis retinal haemorrhages would be induced easily just like Eales s disease

As noted in the opening paragraph it is known that there are various kinds of clinical type in recurring intraocular haemorrhage caused by indefinite etiology Therefore, the mechanism of retinal haemorrhage was analysed in various ways and it was concluded that the structure of vascular walls and the components of the blood might play an important role

From these clinical and histo pathological findings, it may be supposed that the haemorrhages are caused from various factors

tary tract the cardiovascular, urinary hematopoetic and other systems and that it damages the connective tissues and is responsible for a multiplicity of cutaneous disorders The role played by tuberculin type hypersensitivity and chronic infection is an important one for it can enormously intensify tissue damage and destruction It is well known that the local hypersensitivity response to tuberculo protein antigen in this type of hypersensitivity is delayed and prolonged The prevention of the hypersensitivity reaction by desensitization with old tuberculin is now rarely done because of the risk of general and focal reactions

If the inflammation in the wall of the peripheral veins in the eye is due to a hypersensitivity to tuberculo protein antigen, then the cortico steroids may reduce the allergic reaction as long as therapy is continued It has been experimentally demonstrated that the beneficial effects of steroid therapy are mainly due to an ability to block the tissue reaction to hypersensitivity

Since 1944 the author has had the opportunity to study in detail approximately 60 patients with Eales s disease Most of these patients were young adult males veterans of World War II, and were under periodic observation in a large veterans' hospital Many of them were examined two and three times a year over this period Evidence of healed or active pulmonary tuberculosis was present in approximately one third of the cases and the skin tuberculin test was positive in almost all the patients From this experience it is felt that there are two clinical aspects of the medical treatment of Eales s disease The *first* is the initial treatment of the vitreous haemorrhage or when a subsequent vitreous haemorrhage occur The *second* aspect of the medical treatment is the management of the lesions in the retinal veins and the newly formed capillaries aneurysms etc which are formed usually in the periphery of the retina

GENERAL DISCUSSION OF MEDICAL THERAPY

There is no specific treatment known for Eales s disease Most frequently these patients have been treated in the past as if they were tuberculous by tuberculin desensitization injections and general hygienic measures However further haemorrhages have frequently occurred during the course of tuberculin therapy probably from focal reactions and this form of treatment has not met with uniform success or acceptance The author has experienced such reactions in several patients in whom massive vitreous haemorrhages occurred following a tuberculin injection In Donders (4) comprehensive survey of the entire literature on Eales s disease in 1958 he concludes that there is no certain medical therapy

The specific anti tuberculous drugs do not seem indicated such as thiazolsulfone (Promisole R) streptomycin para aminosalicylic acid and isoniazid because of the apparent lack of active bacterial tuberculous infection in Eales s disease The author treated two cases for prolonged periods in hospital with anti tuberculous chemotherapy and in both

MEDICAL THERAPY OF EALES'S DISEASE*

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*Vancouver, British Columbia, Canada***

Although the condition known as Eales's disease is generally thought to be rare there are few among us who have not had several of these patients to treat and the question of these recurrent hemorrhages into the vitreous frequently proves vexing The general concepts of Eales's disease, experimental production of the disease, etiological pathological concepts, surgical therapy and prognosis are being discussed by other members of the symposium The medical therapy which one employs will be dependent upon one's concept of the etiology of this disease

The history and findings are so similar that the author (1, 2) concluded the disease should be considered a clinical entity and not a manifestation of many diseased conditions There are haemorrhages from the peripheral retinal veins, perivascular exudation alongside the walls of the veins and, in many instances, haemorrhages into the vitreous It was postulated that the haemorrhages and exudation resulted from a local hypersensitivity reaction in the walls of the peripheral retinal veins in individuals who have been sensitized to tuberculo protein antigen

Three eyes were available for pathologic study Two had been removed when the patient died from tuberculosis and one when glaucoma supervened In the latter case no signs of perivascular inflammatory process were found, while in the first two eyes a non-specific lymphocytic cuffing was noted Study of the pathologic material revealed that some of the retinal vessels were surrounded by a few lymphocytes but on the whole there was little, if any, inflammatory reaction around the vessels A true inflammatory periphlebitis was not present There were no granulomatous reactions around the vessels and no tubercle bacilli were found in the studies with specific staining The pathologic findings were compatible with the hypothesis that the disease has an allergic basis

Rich (3) has demonstrated that the hypersensitivity state can produce serious disturbances in the respiratory tract and in the alimen

* Read at the XIX International Congress of Ophthalmology New Delhi Symposium on Eales s Disease December 5th 1962

** From the Department of Ophthalmology University of British Columbia and the Department of Ophthalmology Shaughnessy Hospital Department of Veterans Affairs Vancouver British Columbia Canada

In certain patients where the vitreous haemorrahge does not absorb sufficiently within months consideration may be given to vitreous replacement according to the method of Shafer (10) The author has used this treatment in several patients with remarkable success and for no explainable reason with equal failure in others with the onset of phthisis bulbi

(b) *Management of Lesions in the Retinal Veins After Absorption of Vitreous Haemorrhage*

In this stage of Eales s disease the author has advocated the use of subconjunctival injections every two or three months of steroid cortisone, hydrocortisone acetate or prednisolone 25 mg in 1 cc The patients selected for this treatment were those who showed signs of activity of the periphlebitis in whom retinal haemorrhages could be observed ophthalmoscopically in the periphery of the retina As long as haemorrhages in the retina were noted the disease was considered to be active but when haemorrhages did not occur the condition was thought to be inactive As many as eighteen subconjunctival injections have been made in a single eye over a four year period without ill effect It was observed that the steroid usually required two to three months to become absorbed from beneath the conjunctiva but in some patients the residue deposit would be absorbed in five to six weeks

The author has advocated the use of subconjunctival injections of steroid locally in order to reduce the possibility of flaring up an inactive systemic pulmonary tuberculous infection He has felt that the local use of steroid subconjunctivally probably suppresses the allergic response in the walls of the peripheral retinal veins This opinion was supported by the clinical observations in these patients in whom no further vitreous haemorrhages occurred in the majority of patients so treated Periodic observation is necessary in order to determine if the lesions are proliferating with gradual enlargement of newly formed venous aneurysms in patients with Eales s disease This type of case is the phase of the disease probably most satisfactorily treated by photocoagulation

During the past two years the associates of the author at the *Banting Institute* University of Toronto have been studying experimentally the total ocular uptake and routes of penetration of C(14) labelled hydrocortisone following subconjunctival administration in an attempt to determine the depth of penetration and amount of drug taken up by the individual layers of the eye and also the manner of spread from the depot site These studies are being carried out in rabbits by Drs Basu Gornall Wine and Drysdale, and are currently underway The preliminary observations indicate that only a very small amount of the subconjunctival depot of steroid actually enters the eye Disappearance of the steroid deposit from the subconjunctival location appears to occur within seven days The studies are being continued with the development of a radio autographic technique to visualize the route of penetration into the eye and its tissue locali

patients recurrent vitreous haemorrhages occurred while on maximal chemotherapy medication Hogan, (5) in a personal report, studied eight patients with long term anti tuberculous chemotherapy without noting any improvement in the condition

Many other methods of medical therapy have been advocated for Eales's disease, including potassium iodide orally or intravenously as sodium iodide, proteolytic enzymes, thyroid extract, and estrogenic hormones as well as androgenic hormones, all of which the author does not advocate Ascorbic acid has been advocated by many authors as well as rutin and dicoumarol The choline derivatives are considered to have a lipotropic effect on tubercle bacilli and an anti-haemorrhagic effect but opinions about its value are most uncertain The use of cobra venom is also open to differing opinions

Radiation therapy to the posterior segment of the eye has been employed by numerous authors (6, 7) Reese and Jones (8) report favorable results in an eight and ten year follow up of patients with Eales's disease treated by roentgen therapy However, the author treated two patients with roentgen therapy with doubtful success

SPECIFIC TREATMENT OF EALES'S DISEASE

(a) *Treatment of the Patient with a Vitreous Haemorrhage*

Usually the patient first presents himself at the time of the initial spontaneous vitreous haemorrhage As is well known, these patients are usually in good health However, a complete medical examination is indicated, including X ray examination of the chest, skin tuberculin test, complete blood studies, especially in regard to sickle cell anaemia, neurological examination and peripheral vascular studies regarding the possibility of Buerger's disease

The author feels that a patient with a vitreous haemorrhage should be admitted to hospital for complete bed rest and the eyes relatively immobilized either with bandages or pin hole spectacles Given optimal conditions the vitreous haemorrhage is likely to largely absorb relatively quickly with the rapid return of normal central vision The haemorrhage will settle to the lower portion of the vitreous and within one to two weeks the fresh haemorrhage changes in appearance and there are many flocculent appearing white opacities in the inferior portion of the vitreous If there are no signs of active systemic tuberculosis on careful medical examination, the author advocates intensive ACTH therapy intravenously over a ten day to two week period while the patient is in bed in hospital Twenty to thirty mg ACTH in 500cc of distilled water are administered intravenously by means of a slow drip over a five to eight hour period each day With the absorption of the vitreous haemorrhage a careful ophthalmoscopic examination usually reveals the site of the haemorrhage to be from a peripheral or mid peripheral retinal vein Should a subsequent vitreous haemorrhage occur, the patient is re admitted to hospital and the course of ACTH therapy repeated in order to provide maximal block of the hyper sensitivity state to tuberculo protein antigen

TRANSCLERAL DIATHERMIC COAGULATION IN EALES S DISEASE

A FRANCESCHETTI

Geneva (Switzerland)

We have been using surface diathermocoagulation in the treatment of Eales's disease at the Geneva Clinic since 1947 We adopted this procedure for two reasons first because all medical treatment suggested had proved inefficient in most instances This is hardly surprising in view of the lack of accurate knowledge as to the etiology of the disease This holds true for all disorders in which the patient s condition and constitution seem to play the most important role as in our opinion is the case in Eales s disease

The second reason was the high success registered by *Weve* (1939) with diathermic coagulation in the treatment of angiomatosis of the retina and certain chronic peripheral retinitides (probably including some benign cases of Eales s disease)

On several occasions we have had the opportunity of speaking about the results obtained by this new technique which gradually caught on such an extent that the destruction of retinal foci in haemorrhages into the vitreous of young patients regardless of the method used has now become the therapy choice (*Franceschetti* 1 and *Forni*, *S*, 1954 *Franceschetti A* 1955 *Franceschetti*, *A* and *Forni S* 1954, *Forni S* 1958 *Ricci* 4 1959)

Since *Meyer Schwickerath* (1956) developed his remarkable instrument a few years ago, we have been able to destroy affected areas by photocoagulation

The time has come to attempt a definition of the indications and possibly the advantages of one or the other of these two operatory techniques

The principal merit of photocoagulation is accuracy It therefore offers the advantage of making it possible to limit destruction sharply and to approach the central area without great risk of jeopardizing sight It is of incontestable utility in dealing with the insufficiencies which may appear at the edge of diathermically coagulated areas

Moreover it is the only method by which vessels in the vitreous can be destroyed

We reserve diathermy for

(a) *the coagulation of extensive areas*

If an entire quadrant or the entire periphery is to be destroyed, we consider that diathermy has the advantage of simplicity, speed and,

zation Of major interest is whether the steroid can actually diffuse through sclera underlying the depot site into the individual ocular layers

CONCLUSIONS

1 There is no specific medical cure known for Eales's disease at the present time

2 The author is of the opinion that the disease is a manifestation of allergy to tuberculo protein antigen elsewhere in the body

3 Medical treatment basically should be directed towards blocking this hypersensitivity state The judicious use of steroid therapy either locally or systemically seems a rational way of attempting to accomplish this end

4 Further experimental studies are necessary in order to determine whether subconjunctival depots of steroid actually diffuse through the sclera and are capable of blocking locally the hypersensitivity state in the wall of the peripheral retinal veins

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We reserve diathermy for

(a) *the coagulation of extensive areas*

If an entire quadrant or the entire periphery is to be destroyed, we consider that diathermy has the advantage of simplicity, speed and

if appropriately carried out, above all of generally causing relatively few secondary reactions and, in particular far less exudative phenomena

(b) *the coagulation of peripheral areas*

It is often difficult to focus on these areas with the photocoagulator and it is therefore to achieve far easier coagulation diathermically

(c) *the coagulation of detached areas*

For which there is an absolute contraindication to photocoagulation which, for physical reasons, cannot be achieved

(d) *coagulation under unfavorable visibility conditions*

Because of a cloudy vitreous, exudates for which the sight accuracy of photocoagulation cannot be justified or applied

(e) *patients who have not the possibility to be under regular control*

These cases have in general a bad prognosis as photocoagulation will not be done in time if near areas are affected On the contrary, extended diathermocoagulation prevents in general *recurrent* haemorrhages

(f) *overcast skies" coagulation (coagulation "a ciel couvert")*

In extensive haemorrhage into the vitreous where destruction *of entire suspected* areas as well as an attempt to improve resorption of the haemorrhage are indicated The technique itself is not new and is closely related to that for detachment of the retina, however, with the *important* reservation that the zones to be coagulated, after exact *localization, can be very slightly parchmented,* if necessary under ophthalmoscopic control With very weak intensities, there is always a *whitish* exudate *sometimes bordered by minute haemorrhages* which resorb and have no tendency to invade the vitreous The after *effects of the* operation are always extremely *slight Important* post operatory measures are keeping both eyes bandaged for five days and bed rest

Although in performing the overcast skies operation coagulation more often than not covers and extensive area about 14 mm from the limbus, we always try to base our procedure both on the case history and on whatever information the patient's regular ophthalmologist may be able to supply concerning the main location of the lesions at the time when it was still possible to explore the fundus We have already cited the happy turn events may take with this procedure Evidently there is sometimes a direct relation between diathermo *coagulation and the rapid clearing up the* vitreous, which had often remained opaque for several months Very often, within a few days after the operation, the *fundus becomes* visible and in favourable cases, patients recuperate sufficient visual acuity

In 1958 we cited three similar cases Since then, in ten cases where there was perception of light, this procedure resulted in five instances in rapid resorption of the *blood* exudates in the vitreous body

Scientific symposia and symposia read at the XIX International Congress of Ophthalmology held at Delhi from 2nd December to 7th December 1962

PRINTED IN INDIA

BY PYARELAL SAH AT THE TIMES OF INDIA PRESS BOMBAY AND EDITED AND PUBLISHED BY DR Y K C PANDIT BOMBAY MUTUAL BUILDING SIR PHIROZSHAH MEHTA ROAD BOMBAY

Forgacs an assistant at the Geneva Clinic studied the effect of surface diathermocoagulation on the resorption of intra vitreous haemorrhages on rabbits These experiments which will be published shortly confirm clinical observations Although the action of diathermocoagulation was not determined Forgacs was able to demonstrate the same phenomenon as observed in man It should be pointed out that we distinguish between two types of treatment *prophylactic* in which diathermy is applied to lesions which have not yet caused haemorrhages into the vitreous and *therapeutic* intended for more serious cases in which haemorrhage has already occurred With present techniques it is obvious that prophylaxis will, more often than not be reserved for photocoagulation whereas therapy will most often make use of diathermocoagulation

Thus prior to 1959 we had treated 6 cases prophylactically with diathermy five successfully as confirmed by time Since then cases of this type have been reserved for photocoagulation

Our statistics since 1947 comprise 48 cases covering 64 eyes operations

Diathermy was applied 46 times and photocoagulation alone or combined with diathermy was used for the remainder

We will conclude by noting once more that the destruction of affected areas in Eales s disease appears to us to be the only method at present offering satisfactory encouraging results Results would probably be better still if on appearance of the symptoms use were made of these techniques which up to present time have proved absolutely safe

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EALES'S DISEASE
TREATMENT WITH LIGHT-COAGULATION

G MEYER-SCHWICKERATH

Essen Germany

Encouraged by reports of VERHOEFF and FRANCESCHETTI on the favourable influence of diathermy coagulation in Eales's Disease I started light coagulation treatment in 1954 Since then 139 patients (176 eyes) have been treated

TECHNIQUE OF TREATMENT AND NORMAL FOLLOW UP

The technique of treatment has altered during the course of time I shall now describe it in the same way as it is carried out today

The pupil is maximally dilated and the eye is anaesthetized by means of a retrobulbar injection of 5 cc Novocain with hyaluronidase *All* aneurysms and newly formed vessels must be coagulated They can often only be seen at first in their actual extension *during light coagulation* We therefore make a new sketch after this treatment in which the coagulated vessels are recorded Fortunately *the changes in the vessels, above all in the early stages, lie in* the periphery of the retina, so that the resulting defect in the visual field is only small The coagulation is easy if the vessels lie in the level of the retina and are not covered with exudate or haemorrhage It is dangerous and unnecessary to coagulate the dilated and curved vessels, which end in peripheral aneurysms and coils of vessels After the coagulation of the aneurysms these vessels resume their normal structure In cases of proliferation of vesseltrees into the vitreous one can try to close off the arterial and venous roots of these trees by coagulation

The intensity of the light coagulation can be especially low in cases of Eales s Disease It is mostly enough if less than the basic power I, is used, *i e* that the iris diaphragm is closed for some degrees *The intensity is sufficient when, in half a second, a fairly whitish colouring* of the retina in the region of the vessels occurs The vessels themselves *hardly change their appearance at all First in the course of* 2–3 weeks one recognizes whether they are completely closed and have been resorbed

After 4–6 weeks we make another thorough examination in order to see whether any aneurysms are still visible If this is the case, these changes have to be treated again with light coagulation

As a rule we coagulate not more than one quarter of the retinal circumference If larger regions in the periphery of the retina are

affected then we leave an interval of 2 weeks between each coagulation treatment

The further course is marked by the fact that smooth vessel free scars develop in the coagulated region The retinal vessels leading to the scars have a normal size and a normal course After the coagulation of all visible aneurysms has been carried out, check up examinations are made from time to time If new proliferations take place these will again be treated They often occur in regions of vessels which one would least suspect but hardly ever in the region of the old scars

STATISTICS OF CASES

The following statistics contain also cases from the first years in which we had very little experience and in which coagulation was insufficient — according to our opinion today There are also cases in which only a part of the peripheral vessel changes was visible and coagulated whereas others were completely hidden by hæmorrhage

During the time from March 1954 until the end of June 1961 (1954–1959 in Bonn 1959–1961 in Essen) 139 patients (i e 176 eyes) with Eales s Disease were treated with light coagulation Out of these we could follow the course of 114 patients (22 women and 92 men), i e 146 eyes In 3 eyes light coagulation was used to heal a detachment due to Eales s Disease There remain therefore only 143 eyes

67% of the patients were bilaterally affected (DODEN gives 70%)

27 patients were blind in one eye from the same disease and 5 patients from other or unknown causes

In 99 eyes one or several severe vitreous hæmorrhages had occurred before the treatment

16 patients had an iritis earlier or one which was still persistent during the treatment

The number of light coagulation treatments carried out is

in 71 eyes	1 session
in 38 eyes	2 sessions
in 22 eyes	3 sessions
in 12 eyes	4–8 sessions maximum

During an observation period of 1 year minimum 8 years maximum average period 2 9 years 124 out of 143 treated eyes remained without further hæmorrhages

Out of the 124 symptom free eyes there are 12 with a decrease in visual acuity due to traction and exhudative degenerative processes in the region of the macula and one eye with a dense cataract behind which the retinal process most probably has settled down

The 19 eyes in which further symptoms occurred are on the whole very severe and progressive cases Mostly the aneurysmal changes

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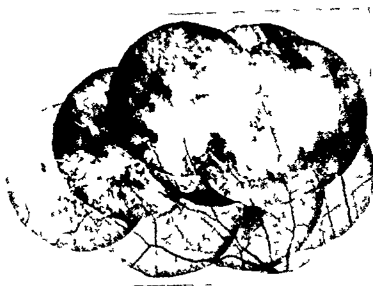


FIG 4 The same area as Fig 3 6 weeks after photocoagulation The coagulated aneurysms are replaced by a smooth scar which is nearly free of vessels A comparison with Fig 2 and 3 shows that the enlarged feeding vessels regained a normal calibre

of the periphery had already advanced very far almost to the centre or there were extensive proliferations into the vitreous

Complications

(1) HAEMORRHAGES

Haemorrhages occuring during coagulation can mostly be brought to a standstill by immediate coagulation of the blood 4 severe vitreous haemorrhages occurred during the coagulation and could not be stopped They have all been resorbed except in one case There were five small vitreous haemorrhages during the first week after the treatment In all cases a quick resorption followed

Smaller pre retinal haemorrhages can be very often seen in the first two weeks after light coagulation It is often only due to the absorption of the coagulated aneurysm

Other haemorrhages which have occurred through new non coagulated aneurysms or due to insufficient coagulation are not mentioned here They are considered under the failures

(2) RETINAL DETACHMENT

A detachment of the retina was seen nine times during or after the treatment with light coagulation With the exception of one case we are dealing with very progressive cases with vitreous tractions

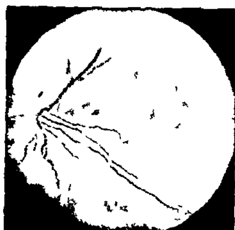


FIG 1 Arterious venous net work 3 days after photocoagulation

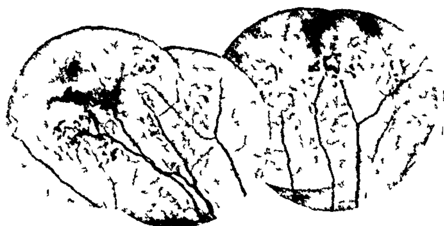


FIG 2 Typical appearance of Eales's Disease in the tempero-superior periphery with aneurysms and short cuts



FIG 3 The same area as FIG 2 4 days after photocoagulation

We presume that abnormal development of vessels is present also in Coats's disease and in Miliary Aneurysms Retinitis These two diseases are also progressive and sometimes accompanied by an iritis In early stages the affected vessels can be destroyed by light coagulation and thus the disease is brought to a standstill

Summary

Encouraged by VERHOFF'S and FRANCESCHETTI'S reports on the favourable influence of diathermy coagulation in Eales's disease I have treated 139 patients i e 176 eyes with light-coagulation from 1954 to 1961

Out of 143 eyes whose course could be followed over an average of 2 9 years 124 eyes remained without any new haemorrhages

Experience has shown after destroying the vessel proliferations and arterio venous aneurysms that not only any haemorrhage is missing but that also the tendency to new proliferations disappears in the region of the coagulated vessel

Observations of the first apparent stages have shown that the disease begins with dilated arterio-venous vessels (shunt-capillaries) in the peripheral retina The process proceeds by development of further arterio-venous aneurysms from the periphery in the direction of the center of the retina It leaves behind a vessel free region in the peripheral retina The ophthalmoscopical observations may be explained by the fact that a capillary closing process (*in outbursts*) is the beginning of the disease which may be embolitic thrombotic or of endangitic nature This progresses independently further through a circulus vitiosus between hypoxaemie and vessel proliferation

The favorable influence of light coagulation can only be explained in the following way that the circulus vitiosus is interrupted by the destroyed aneurysms and/or that the resulting scars do not give any fresh stimulation for proliferation of new vessels

The coagulation of aneurysms cannot hinder the fact that new proliferations occur in other vessel regions previously unaffected These must be coagulated again in order to prevent fresh haemorrhages

In the treatment of Eales's disease by light-coagulation different complications occur (haemorrhages detachments macular degenerations) which obviously cannot always be avoided

In spite of these complications I would like to recommend light-coagulation therapy in Eales's disease It leads in most cases to a clinical cure of this disease

and proliferations Three cases could be re attached by scleral re section and 1 case by girdle suture

In 8 eyes there was a retinal detachment before the treatment In 6 eyes the operation was a success so that they could be followed by coagulation of the aneurysms

From this number it follows that the operative prognosis of detachment due to Eales's disease has improved since we have treated these cases by volume reducing operations

(3) POSTCOAGULATIVE MACULAR DEGENERATIONS

This peculiar macular process occurred not only in patients with Eales's disease but also in others, which have been treated by diathermy or light coagulation for other reasons This disease has been known for a long time as the so called "distance injury" of the macula after diathermy operation R BRÜCKNER has recently reported on an interesting observation concerning this

The process begins mostly a few weeks up to two months after light coagulation has been carried out Sometimes the visual acuity improves after antiphlogistical therapy with Cortison, Butazolidin or Tanderil In many cases there still remains a large permanent central scotoma We experienced these complications 5 times in a severe form (visual acuity less than 5/50) and 4 times in a less severe form (visual acuity better than 5/50)

This complication is the more serious because in all cases it does not concern a very advanced or complicated form In all cases the visual acuity was normal or practically normal before the treatment

How can one explain the surprising effect of light coagulation in Eales s disease?

The sickle cell haemoglobin C retinopathy shows us that quite a similar process may arise through multiple microemboli It seems to be possible that an obliterating or obturating process in the shunt capillaries of the peripheral retina appears also at the beginning of the so called Eales's disease This process once brought into action could become *independent and then progress in a circulus vitiosus* of hypoxaemia and proliferation from the periphery to the centre The circulus vitiosus will be interrupted by the coagulation of the aneurysms At the same time a scar tissue with a low oxygen supply is developed The inflammatory and degenerative appearances characterizing the *later stages of the disease should only then be considered* as the consequence of an disturbed haemodynamic

Developmental anomalies of retinal vessels, especially in the peripheral retina, can obviously bring into action quite a similar picture

It is well-known, that the clinical picture of the Varyx Aneurysmaticus Retinae may proceed and lead to a similar final stage as in Eales's disease We have observed 4 cases of this type

5 Syphilis — only two patients out of 100 had this lesion which was coincident It does not cause haemorrhage though it involves every structure of the body including eye Rather it causes endarteritis obliterans
6 Anaemia — none of our patients had anaemia of a severe degree to cause haemorrhage
7 Malaria — The disease in our country is definitely on decrease and is not restricted to males
8 Blood calcium deficiency — only 2 cases had low Blood calcium
9 Environmental disturbances — This is the result and not the cause of the disease
10 Tubercular periphlebitis
11 Endocrinal disturbances
12 Retinal perivasculitis

In my opinion the lesion is caused by allergy due to tuberculo proteins The positive skin Tuberculin Test in patients is more worthy in view of survey of tuberculin tests in younger adults of comparable age group which indicate that only 25 to 40% cases are positive It seems that the patient with recurrent intra ocular haemorrhage has become sensitized to Tuberculo proteins and a local state of hypersensitivity has developed in the walls of retinal veins with resultant exudation and haemorrhage

Regarding mode of infection reaching the eye, the infection travels through the blood vessels and the organism penetrates through the small arterioles reaching the perivascular tissues of small veins to cause periphlebitis In my opinion the infection gets lodged in the ciliary body where it reaches via blood stream and either the bacteria themselves or the toxins produced by them pass via the vitreous to act upon the blood vessels causing periphlebitis

I do not think that local retinal perivasculitis at the periphery causing neovascularization which may be inter retinal uveal or vitreal can explain the course of events leading to rupture causing recurrent intra-ocular haemorrhage It was present only in 12 out of 100 cases

As to why the condition is rare in females than in males 1 to 25 can not be explained by above etiology as tubercular periphlebitis and retinal perivasculitis are quite common in them

Glandular disturbances may be playing an important role about which we know very little

FAMILY HISTORY

Only 6 patients gave positive history of tuberculosis in the family stating that their parents were admitted in T B sanitorium

EALES'S DISEASE—ITS ETIOLOGY & PROGNOSIS

Dr S P GUPTA, F R C S, (Ldin), D O M S, (Lond),
Professor and Head of the Department of Ophthalmology,
King George's Medical College, LUCKNOW,
and Chief Ophthalmic Surgeon,
Gandhi Memorial & Associated Hospitals,
(Lucknow, India)

The following conclusions have been derived from 100 cases of Eales's disease treated privately and in King George's Medical College, Lucknow

INCIDENCE

The disease though world wide is more common in tropics and in our series average age was 23 9 years youngest in a child aged 15 years *and eldest male 48 years*

It is more common in males than females ratio in my series is 25 *to 1 Mostly patients belonged to low income group* were field workers and were of active habits Out of our series of 100 cases of Eales's disease the classification is as follows

Field workers	40	
Clerks	20	
Students	20	(3 were medical students)
Businessmen	10	
Policemen	6	
Housewives	4	
	100	

ETIOLOGY

A large number of conditions have been mentioned as the cause of Eales's disease

1 Akin to thrombo angitis obliterans or erythema nodosa
2 Septic foci in teeth, tonsils or other parts of Body
3 Helementhiasis — 50% of cases mostly field workers and clerks had ankylostomiasis infection This is very common in our country chiefly in those residing in rural areas or in unhygienic conditions *in the urban areas*
4 Vitamin deficiency — none of vitamin deficiency is directly or indirectly *related to this condition*

FREE PAPERS

Lids Conjunctiva Lacrimal Apparatus

Uvea and Lens

Retina and Optic Nerve

Cornea

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4 Vitamin deficiency — none of vitamin deficiency is directly or indirectly related to this condition

Out of these 84 cases reported sudden loss of vision and 16 cases only gradual loss of vision

Only 12 cases out of 100 showed neo vascularization

Above cases were divided for treatment in three broad groups with complete rest in bed

1 50 Cases treated by antitubercular treatment consisting of Dihydrostreptomycin I GM O D for 1 month, Tibizide 50 mgm B D for one month, and subconjunctival strepto mycin 1 cc twice a week

2 25 Cases put on coagulant therapy consisting of Calcium gluconate with vitamin C' 10% 10 cc A D such 15

Hemostic tab or
Stryptobion or } 1 Tab B D
Claudin

3 25 Cases put on endocrinal therapy — Testosteron Propionate starting with 5 mgm increased to 10 mgms on alternate days intra muscular for one month

I have not tried light coagulation therapy

We found that patients put on anti tubercular treatment with subconjunctival streptomycin behaved better and only in 6 cases recurrence was present Of course anti tubercular treatment should be repeated after every 4 months Such three courses should be given and patient advised to carry on light work and not do manual work

Prognosis will also depend on the stage at which patient has presented himself first time and the period that has elapsed before the treatment has been started We have found that prognosis was worse in cases which had recurrent haemorrhage or which presented them selves with old iridocyclitis chorio retinitis or where retinal detach ment has occurred due to formation of fibrous bands (Retinitis Proli ferans) The younger the age of patients worse was the prognosis

The prognosis was better in cases put on anti tubercular treatment with subconjunctival treatment repeated after 4 months Very few cases presented themselves with Retinal perivasculartis and no haemorrhage I have no experience of light coagulation therapy which is still not much in use in our country as treatment of Eales s disease

FURTHER INVESTIGATIONS

W R and Kahn positive in 2 out of 100 cases blood calcium, Blood Serum, prothrombine normal except in 4 cases

Urine, W B C count, haemoglobin and differential count normal examination of Stool (revealed ankylostomiasis infection in 50 cases)

Sinuses were normal except in 4 cases

Only 3 eyes were enucleated as the eyes were blind

Histopathological examination revealed tubercular lesions, — epitheloid and giant cells

Constipation and headache does not seem to be important features of the disease

Though Henry Eales laid great stress on it and he did so to bring the symptomatology of the disease in line with hypothesis of alimentry and circulatory neurosis Probably his patients were cases of sinus trouble or other conditions giving rise to headache which is quite common

The mental state being in low spirits seems natural in a young man whose visual acuity in either or both eyes is being repeatedly interfered with and each time going down due to irreversible changes

A young man with prospects of living in this world without good vision will not keep himself in high spirits This was clearly noticed in three medical students who became neurotic and in low spirits with each attack of haemorrhage In my series of cases none had high blood pressure

FIRST EYE AFFECTED

In our series right eye was affected in 66 and left eye in 34 cases Eighty of them took treatment as soon as first eye got affected, all of them reported for check up Second eye was not affected in these cases In twenty cases other eye was affected the interval being 6 months to 2 years

The recurrence has no relation with the eyes which got first affected Sometimes the eye which was affected first showed less recurrence than the eye that was affected late Eighty four cases reported sudden loss of vision

MANIFESTATIONS—ITS RELATION TO PROGNOSIS

Review of 100 Cases

1 Usually the patients manifest first with periphlebitis and retinal and vitreal haemorrhage — 84 cases

2 Manifest as branch *venous thrombosis leading to* haemorrhage — 10 cases

3 Manifest as chronic iridocyclitis or chorio retinitis and then leading to vitreous haemorrhage — 6 cases

The table indicates that about 3/4 of all the eyes can be saved in this way In addition it demonstrates, that light coagulation in Eales's disease gives the best results when performed during the initial stages of its development Under these conditions there were only few failures in relation to the successful cases, viz 4 against 23, i e 1 6 in the first group This correlation decreases in the second group, here were 4 failures to 14 good cases, i e about 1 3,5 In the third group are found 6 failures against 4 cured cases, this corresponds a relationship of 1 0, 66 In this latter group the failures predominate remarkably

It is to be concluded therefore that light coagulation as treatment of Eales's disease should be done as early as possible The practical value and importance of light coagulation in Eales's disease may also be demonstrated by the following history A young man suffering from bilateral Eales s disease (group I) was coagulated on his right eye and is considered to be cured over more than one year Unfortunately, he refused the treatment on his left eye and the left eye is now blind by recurrent hæmorrhages

One of our advanced cases had a delayed hæmorrhage in the vitreous and two had delayed retinal detachment In the early stages however we could find no complications which would contraindicate light coagulation as a treatment of choice in that otherwise hopeless disease

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SIGNIFICATION DE LA POLYGLOBULIE ET DE L'HYPER COAGULABILITE DANS LA PATHOGENIE ET LE TRAITEMENT DE LA MALADIE d EALES

JOSÉ CASANOVAS

(*Barcelona*)

En collaboration avec Mrs Castillo Farreras et Olivella nous avons demontre la grande frequence de la polyglobulie dans la periphlebite retinienne Sur 59 patients 28 c est a dire la plus grande partie avaient plus de 5 millions d hematies par centimetre cube Les valeurs de l hematocrite etaient souvent alterees, on trouvait habituellement la vitesse de sedimentation globulaire diminuee fait normal dans les polyglobulies mais aparentmment paradoxal chez les malades qui souffraient un proces inflamatoire actif

Dans la production des thromboses en general peuvent intervenir l hypercoagulabilite l estase et les alterations de la paroi vasculaire Dans les *trombophlebites* retiniennes du syndrome d Eales interviennent surtout les alterations vasculaires (periphlebite et phlebite) Bien que, dans quelques cas l hypercoagulabilite ne soit pas le facteur pathogénique le plus important toutefois, il reste le plus accessible

DISCUSSION

TREATMENT OF EALES'S DISEASE BY LIGHT COAGULATION

W BÖKE,

(Germany, Munster Westf)

There is no doubt, that light coagulation is a unique and effective method of treating Eales's disease May I give some personal experience and results with it over the past four years, including a total number of 55 eyes in 43 patients Post operative observation was maintained in 53 eyes and all the cases were classified in 3 groups according to the severity of disease as viewed by ophthalmoscopy

The *first group* was called " initial alterations ", *i e* small haemorrhage spots and exudates along the retinal veins, dilatation and tortuosity of the peripherial vessels and new formed retinal vessels as well

Group No 2 consists of the retinal features of group No 1 plus the additional findings of recurrent vitreous haemorrhage

The *third group* were the poor cases, wherein we found the characteristics of group No 2 complicated by neovascularization of the vitreous, retinal detachment or secondary glaucoma

The end result is as follows

	Eyes	+	(+)	—	?
Group I	27	22	1	4	—
Group II	18	10	4	3	1
Group III	10	2	2	5	1
	55	34	7	12	2
		41		14	

\+ = absolutely successful cases *i e* practically healed cases without recurrences

(+) = good results remarkable improvement the final result however, is not yet sure

— = no success recurrent haemorrhages neovascularization of the vitreous retinal detachment *etc*

? = patients did not return for follow up studies

The table indicates that about 3/4 of all the eyes can be saved in this way In addition it demonstrates that light coagulation in Eales s disease gives the best results when performed during the initial stages of its development Under these conditions there were only few failures in relation to the successful cases, viz 4 against 23 i e 1 6 in the first group This correlation decreases in the second group here were 4 failures to 14 good cases, i e about 1 3,5 In the third group are found 6 failures against 4 cured cases this corresponds a relationship of 1 0, 66 In this latter group the failures predominate remarkably

It is to be concluded therefore that light coagulation as treatment of Eales s disease should be done as early as possible The practical value and importance of light coagulation in Eales s disease may also be demonstrated by the following history A young man suffering from bilateral Eales s disease (group I) wa coagulated on his right eye and is considered to be cured over more than one year Unfortunately he refused the treatment on his left eye and the left eye is now blind by recurrent hæmorrhages

One of our advanced cases had a delayed hæmorrhage in the vitreous and two had delayed retinal detachment In the early stages however we could find no complications which would contraindicate light coagulation as a treatment of choice in that otherwise hopeless disease

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SIGNIFICATION DE LA POLYGLOBULIE ET DE L'HYPER COAGULABILITE DANS LA PATHOGENIE ET LE TRAITEMENT DE LA MALADIE d EALES

JOSÉ CASANOVAS
(*Barcelona*)

En collaboration avec Mrs Castillo Farreras et Olivella nous avons demontre la grande frequence de la polyglobulie dans la periphlebite rétinienne Sur 59 patients 28 c est a dire la plus grande partie avaient plus de 5 millions d hematies par centimetre cube Les valeurs de l hematocrite etaient souvent alterees on trouvait habituellement la vitesse de sedimentation globulaire diminuee, fait normal dans les polyglobulies mais aparentmment paradoxal chez les malades qui souffraient un proces inflamatoire actif

Dans la production des thromboses en general peuvent intervenir l hypercoagulabilite l estase et les alterations de la paroi vasculaire Dans les trombophlebites retiniennes du syndrome d Eales interviennent surtout les alterations vasculaires (periphlebite et phlebite) Bien que, dans quelques cas l hypercoagulabilite ne soit pas le facteur pathogenique le plus important toutefois, il reste le plus accessible

DISCUSSION

TREATMENT OF EALES'S DISEASE BY LIGHT COAGULATION

W BÖKE,
(Germany, Munster Westf)

There is no doubt, that light coagulation is a unique and effective method of treating Eales's disease May I give some personal experience and results with it over the past four years, including a total number of 55 eyes in 43 patients Post operative observation was maintained in 53 eyes and all the cases were classified in 3 groups according to the severity of disease as viewed by ophthalmoscopy

The *first group* was called " initial alterations ", *i e* small haemorrhage spots and exudates along the retinal veins, dilatation and tortuosity of the peripherial vessels and new formed retinal vessels as well

Group No 2 consists of the retinal features of group No 1 plus the additional findings of recurrent vitreous haemorrhage

The *third group* were the poor cases, wherein we found the characteristics of group No 2 complicated by neovascularization of the vitreous, retinal detachment or secondary glaucoma

The end result is as follows

	Eyes	+	(+)	—	?
Group I	27	22	1	4	—
Group II	18	10	4	3	1
Group III	10	2	2	5	1
	55	34	7	12	2
		41		14	

\+ = absolutely successful cases *i e* practically healed cases without recurrences

(+) = good results remarkable improvement, the final result however, is not yet sure

— = no success recurrent haemorrhages neovascularization of the vitreous retinal detachment *etc*

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Le traitement par le Sintrom sous contrôle a duré de 5 à 30 mois (en moyenne 14). Si nous comparons ces résultats avec ceux du groupe traités par médication anticoagulante, nous obtenons les résultats suivants

	Nombre de cas	*Echecs*	*Cas restés stationnaires*	*Amélio rations*	*Pourcentage des améliora tions*
Sans traitement anticoagulant	36	5	7	24	60 %
Avec traitement anticoagulant	10	2	1	7	70 %

Parmi les cas où l'on a noté une amélioration grâce au Sintrom, l'un d'eux subit une récidive assez notoire au bout de 4 mois, un autre (plutôt inconstant à suivre la thérapeutique) subit quelques récidives insignifiantes. Les autres se sont trouvés délivrés de toute hémorragie nouvelle.

Quand pourra-t-on commencer le traitement anticoagulant en face d'une hémorragie récente? Nous pensons qu'il est toujours plus prudent d'attendre quelques jours après avoir constaté ophtalmoscopiquement l'arrêt de l'hémorragie.

L'écart entre les séances de photocoagulation et l'établissement de l'hypocoagulabilité ne doit pas être si sévère. En fait, l'application correcte de la photocoagulation, selon notre avis, n'entraîne le danger d'hémorragie que dans le cas d'une augmentation patologique de la perméabilité capillaire. De toutes façons, il nous paraît préférable de maintenir le taux de coagulation du patient dans les limites de la normalité durant les jours où l'on pratique la photocoagulation ainsi que pendant les deux ou trois jours précédents. Une fois la photocoagulation terminée on revient aux doses qui nous permettent d'atteindre le degré d'hypocoagulation convenable.

Le traitement anticoagulant n'est pas contraire aux médicaments comme la quercitine et la vitamine C qui renforcent la paroi des vaisseaux: nous associons souvent les deux traitements. De même nous ajoutons aussi des injections sousconjonctivales d'acétate d'hydrocortisone pour lutter contre le facteur hyperergique qui existe d'ordinaire dans la patogénie de la périphlébite.

Nous employons toutes les deux ou trois semaines 1 c c (25 milligrammes) d'acétate d'hydrocortisone qui, avec instilation anesthésique préalable, est très bien tolérée.

celui que nous pouvons modifier le plus facilement grâce à notre thérapeutique. La *polyglobulie* en augmentant la viscosité du sang et provoquant leur ralentissement circulatoire favorise la coagulation intravasculaire.

Outre la numération globulaire, l'hémogramme et les épreuves courantes de la coagulation et de la perméabilité capillaire, nous cherchons toujours *chez nos* patients, le temps de prothrombine et le temps d'héparine.

Le temps de prothrombine (normal 100%) décèle les facteurs extrinsèques, tandis que le temps d'héparine (test de Soulier et de Le Bolloch) décèle les facteurs intrinsèques de la coagulation. Rappelons qu'un indice supérieur à 1, pour le temps d'héparine, indique une *hypercoagulabilité*. Un temps entre 0, 4 et 0, 5 pourrait déjà être dangereux.

Généralement, avec le traitement, les deux valeurs (temps de protrombine et temps d'héparine) descendent simultanément, mais *pas toujours*, surtout au commencement du traitement.

Pour obtenir une hypocoagulabilité convenable nous chercherons à prolonger les deux facteurs mentionnés à 1/3 ou ¼ de leur valeur *normale*. Un abaissement du temps de prothrombine à 4 ou un indice d'héparine à 0, 5 ou 0, 6 seront déjà suffisants.

Pour obtenir l'hypocoagulation, les médicaments les plus recommandables sont, dans notre cas, les cumariniques.

Maintenant, le produit cumarinique que nous employons le plus est le "Sintrom", tablettes de 4 mgrs. de 3 (4' nitrofenil acetil etil) 4 oxicumarine, dont les avantages sont les suivants:

(1) rapide diminution de l'hypercoagulabilité;
(2) une seule dose par jour "per os" suffit pour maintenir abaissée la coagulation pendant 24 heures,
(3) en cas de surdosage, la coagulation se régularise rapidement si tôt qu'on arrête le médicament. Celui-ci possède une accumulation minima.

La posologie est la suivante: les premières 24 heures 4 à 6 comprimés, pendant les 24 heures suivantes, 3 comprimés et à partir du troisième jour on doit régler la dose selon le temps de prothrombine. Pour atteindre un temps de prothrombine de l'ordre de 40 à 30%, c'est à dire le plus convenable, on doit donner un ou deux comprimés par jour. Après quelques temps, 3/4 de comprimé suffisent. Le contrôle du traitement anticoagulant sera fait quotidiennement les trois premiers jours, tous les deux jours pendant la semaine suivante, ensuite deux fois par semaine et dans la suite du traitement, toutes les deux ou quatre semaines.

Parmi les 59 cas de périphlébite rétinienne que nous avons traités depuis 1957, 36 ne l'ont pas été par anticoagulants. Quant aux autres 10, ont été traités avec le Sintrom. Le reste par héparine syntétique sans contrôle méticuleux de la coagulation.

CLINICAL ELECTRORETINOGRAPHY

DISCUSSION

INTERNATIONAL ORGANIZATION AGAINST TRACHC

The therapy was divided into four groups (Table I)

TABLE I

GROUP A
SUBCONJUNCTIVAL HYDROCORTISONE

GROUP B
SUBCONJUNCTIVAL HYDROCORTISONE + ANDROGENS

GROUP C
SUBCONJUNCTIVAL HYDROCORTISONE + METHIONINE AND CHOLINE

GROUP D
SUBCONJUNCTIVAL HYDROCORTISONE + ANDROGENS + METHIONINE CHOLINE

The cases were divided into 4 groups for purposes of evaluation of effectiveness of the therapy particularly in early cases (Table II)

CLASSIFICATION OF CASES

TABLE II

GROUP I
SUDDEN DIMINUTION OF VISION
FUNDUS EXAMINATION REVEALS VENOUS DILATATION
DISCONTINUITY OF VEINS AND PERIVASCULITIS
PRE RETINAL OR RETINAL HAEMORRHAGES

GROUP II
MORE THAN ONE ATTACK OF VITEROUS HAEMORRHAGE
MULTIPLE RETINAL AND PRE RETINAL HAEMORRHAGES
THIN BANDS OF RETINITIS PROLIFERANS
EARLY CHANGES OF PERIVASCULITIS IN THE OTHER EYE

GROUP III
ABOVE CHANGES MORE MARKED

GROUP IV
MARKED RETINITIS PROLIFERANS WITH OR WITHOUT DETACHMENT OF RETINA

Best results were obtained in cases who were given combined therapy (group D) and next in cases treated by group C during the follow up of 6 months to 2 years

The results were assessed on the basis of recurrence rate, period after which recurrence occurred and the residual retinitis proliferans Cases which did show recurrence the period between the attacks was markedly increased after the start of therapy Another significant point noted was that one patient who had attack in one eye and showed slight venous dilatation tortuosity or dipping of veins and discontinuity in the other fundus developed haemorrhage in the second eye during the period he was under treatment

Dans les phases aiguës de la périphlébite et après les photocoagulations, *nous* avons recommandé dans quelques cas la butadione (*Butazolidine*) qui, *en outre*, développe une certaine action anticoagulante.

Il faut se préoccuper de lutter, en même temps, contre les facteurs étiologiques *qu'on pourrait* déceler dans un cas donné : endocrinopathie, allergie à la toxine tuberculeuse, infection *focale*, etc.

On ne doit pas oublier que le traitement anticoagulant n'est pas un traitement étiologique, mais un traitement *prophylactique*.

A ce propos, on peut rappeler que le traitement antituberculeux habituel (streptomycine, hidrazide, etc.) ne modifie pas sensiblement les facteurs de coagulation.

En conséquence, nous estimons que le traitement anticoagulant, appliqué de *la* façon que nous venons d'expliciter, et la *photocoagulation*, restent aujourd'hui les deux éléments les plus importants pour combattre *la* périphlébite rétinienne.

THERAPY OF EALES'S DISEASE

DR MADAN MOHAN
(*Delhi, India*)

Therapy and more so prophylaxis of a disease are more important than any of its other aspects. These largely depend upon the knowledge of etiopathogenesis *of the condition*. The etiology and pathogenesis of *Eales's* disease has so far been speculative and the treatment empirical and shall remain so till the etiology becomes known.

Various forms of treatment advocated and practised, some of them quite contradictory to one another, range from Yogic exercises to absolute bed rest, anti-tubercular and tuberculin treatment, hormones male and female, coagulants and anticoagulants, roentgen therapy, diathermy and last but not the least photocoagulation.

The choice of treatment largely depends upon the facilities available and the interests of the treating surgeon rather than the actual merit of the treatment for they are all as yet under trial.

On the presumptive etiological theory of hypersensitivity to tuberculo proteins Elliot (1954) suggested the use of subconjunctival hydrocortisone. Encouraged by his results and good reports with androgens and choline we did a comparative study of therapy of sixty (60) cases of Eales's disease.

The bleedings of the vitreous body continued and the centers of phlebitis and peri phlebitis were growing steadily worse

The patient became blind on her right eye owing to in inoperable choroidal cataract due to lack of light perception

Her right eye was on the way of following suit having reached the proliferating stage with thick border lines and an organized peri venous and pre papillary plastic reaction

With blindness imminent, and encouraged by the successful intrafemoral treatment of severe disorders in leg and pelvic veins we requested Dr Beheran to consider the application of a similar intra carotidal treatment

The patient agreed to the treatment, duly notified in advance of the danger involved and of the lack of previous experience

Before starting the treatment, the necessary preliminary tests were made to determine whether the patient was able to tolerate the medication involved

Beheran s Technique

After locating the carotidal artery on the patient s neck an 8 gauge needle of an average length of 6 centimeters is plunged into the lumen of the artery The syringe i filled with 10 cc of 1% or 2% novocaine to be injected extremely slowly

The novocaine hould be injected very slowly and intermittently to avoid subjective troubles such as feelings of drunkenness cloudy vision hallucinations loss of consciousness When the shot is over, any symptoms of intolerance abate Should they however be very intense a small intr venous pentothal shot should be administered

If it is done correctly the patient only feels the peripheric distention of the vessels

After the novocaine injection the needle is kept in the artery and the syringe exchanged for another 10 cc one filled with a solution of the desired antibiotic in 5 or 10 cc of physiological serum or distilled water After this shot the vascular section should be compressed for a few minutes whereupon the procedure is finished

The treatment has to be administered on an empty stomach with the patient lying on his back

The shot may be repeated at daily or even hourly intervals

From January through March 1953 Dr Beheran made 7 shots into the right carotid first 3 penicillin shots and later on upon my request because of the doubtful etiological relationship with TB, he switched to streptomycin administering another four shots After a 20 day interval another seven shot were administered

This patient has never again had another haemorrhage since 1953 The treatment ended in June 1953 Last examination 10th November 1960, vision on right eye = 20/200 with correction eye calm vitreous body clean plastic periphlebitic and pre papillary sequel non evolutive Has remained cured for more than 8 years and subjected to annual check ups

Knowing that *the disease tends to be bilateral* (56% in present series) we looked for early changes in the veins in the normal eye and all suspected potential cases (8 in the present series) were given sub conjunctival hydrocortisone at 6–8 weeks interval. None of these developed any haemorrhage during the period of observation of 6 months to 2 years. A prophylactic use of this therapy in the unaffected eye is therefore, recommended.

INTRACAROTIDAL TREATMENT OF EALES'S DISEASE A CONTRIBUTION TO ITS STUDY

DR G VON GROLMAN

Buenos Aires — Argentina

In studying those intra ocular haemorrhagic diseases that are not caused by arteriosclerosis or by hypertension, we have endeavoured for years to determine the importance of the vein factor and of the humoral factor.

This problem has particularly interested us in the case of diabetic retinosis and of Eales's sickness.

Surprised and encouraged by the excellent results obtained with intra femoral therapy in cases of leg and pelvic vein disorders, we have decided to use similar techniques in exceptional cases of diabetic retinosis and Eales's sickness via intracarotidal treatment.

We have tried it out on a few cases of diseased retina due to diabetes — to which I am not going to refer now — and on one case of severe and progressive Eales's sickness which we have followed up for 20 years with exhaustive ophthalmologic studies, both clinical and humoral.

The patient was a 59 year old lady who at that time had been treated by us for 10 years for phlebitis and peri phlebitis of the retina, with repeated haemorrhages of the vitreous body.

In 1943, clinical tests and examinations revealed change of hfi, *focal glomerulonephritis, a slight liver insufficiency, disproteinemia*, blood pressure normal, amaebiasis, rhinopharynx normal, Brussells test negative, no phimic *sequels*, and *a slight pre thrombotic condition*.

I want to point out that the clinical, humoral, focal radiological and other studies have been conducted in an extremely meticulous manner by colleagues who are top experts in their respective fields.

The patient withstood ten years of severe treatment under the strict supervision of the ophthalmologist, the clinician and the hemato logist. The latter (Pavlovsky) treated the slight pre thrombotic *condition* by means of anticoagulants which proved unsuccessful, as did the anti phimics, the liver protectors, the corticoids, and so on.

A survey of 32 cases of Eales's diseases was made at the Eye Infirmary, Medical College Calcutta at present Institute of ophthalmology, during the past 4 years regarding etiology, complications and treatment

MATERIALS

All the cases were obtained from the Eye Infirmary, 32 cases showed involvement of 46 eyes The diagnosis was confirmed on the point of the presence of periphlebitis retinae and retino vitreous haemorrhage A full history was obtained of both general and local conditions Routine etiological investigations were carried out for the presence of tuberculosis (screening X ray Chest E S R & Mantoux test 1 in 100 000) blood tests for syphilis, septic foci (teeth E N T), blood count, B T C T urine stool and blood sugar

Conservative treatments were prescribed for each of them and the effects were followed up The treatment included a combination of the following

(i) Anti tubercular therapy with P A S, Streptomycin and Isoniazid

(ii) Coagulant therapy, with Rutin & Vit C or Calcium gluconate with Vit C or Vit K or styptovit

(iii) Steroid therapy with prednisolone tablets or A C T H 1 in 10 units twice daily or Retrobulbar injection of decadron

Special treatments included — diathermy coagulation of bleeding area of retina and diathermy for detachment

I have prepared a chart with full details of 32 cases but unfortunately that is too lengthy to be shown here However, the salient features may be summarised as follows —

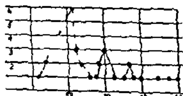
ANALYSIS OF CASES

I Incidence 32 cases out of 25 760 (1 in 805) eye cases seen Reported incidence 1 in 366 (Nederlands Gasthuis voor Ooglijdersat Utrecht)

1 in 1000 to 1500 (Dufour and Gonin)

6 in 29 000 (Paton)

II Frequency with age



maximum incidence at 22 years of age

III Sex 3 of 32 were female



One in every 10

We believe that this is the first case of haemorrhagic vein disorder to be treated and cured intracarotidally, since our bibliographic search for previous records has remained negative

Of course, it opens up a possibility that may become very valuable and likely to be improved by combining according to the requirements of the case on hand, anti infectious with anti coagulant and anti reactive medication

We also believe that intracarotidal treatment may become a heroic measure to be taken in thrombophlebitis of the sinus cavernosus

In the May 1961 issue of the Journal of Angiology, Sussmann and Fitch suggest intracarotidal treatment for administering fibrinolytic enzyme *in treating vascular occlusions in the brain*

Vein pathology plays an outstanding part in R D and in diabetic blindness *There is a very numerous R D group in which treatment* with anti coagulants is formally indicated Their association with fibrinolytic enzymes is worthwhile studying

In very severe cases of retinosis, with relapses of large scale haemorrhages, advanced impairment of vision, persistent damage due to phlebitis and a relative soundness of the arterial system, the indication of intracarotidal treatment should be resorted to as an exceptional and heroic measure after the other methods of treatment have failed

This indication is subject to the extent to which the arterial system has been affected, and to the encephalic and other afore mentioned conditions Intracarotidal treatment is indicated in Eales's sickness *whenever its severity warrants it In cases of thrombophlebitis* of the sinus cavernosus, its early application is worthwhile considering

The *therapeutic requirements* of the vein condition within the eye may be discarded by clinical counter indications, but they ought not to be disregarded because of lack of extra ocular semiological corroboration

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EALES'S DISEASE GENERAL OBSERVATION

DR N N CHANDA
Institute of Ophthalmology,
Calcutta, India

Eales's disease is a fairly common malady in Bengal The interest of the ophthalmologists has been drawn to solve the problem of its etiology and treatment throughout the world but as yet no definite conclusion has been arrived at (P C Donders 1958) Various sorts of treatment were suggested by various workers These included coagulation (diathermy as well as light) of the diseased vessels Apart from symptomatic treatment and treatment of complications other treatments would mean an emphirical one

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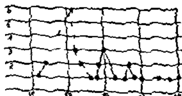
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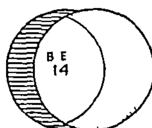
III Sex 3 of 32 were female



One in every 10

IV Ocular preponderance

R E 8



L E 10

left eyes were Only involved in 10 cases

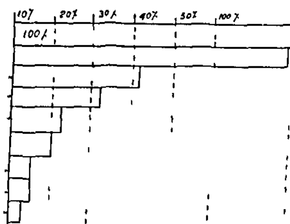
right eyes were Only involved in 8 cases

Both eyes were involved in 14 cases

V Trauma Vague history of previous injury to one eye were obtained in two cases of binocular incidence

VI Feature and Complications

(a) Periphlebitis retinae 100% cases and always peripheral
(b) Retinal haemorrhage 99%
(c) Vitreous haemorrhage 32%
(d) Retinitis proliference 23%
(e) Retinal detachment 13%
(f) Patches of old chorioretinitis 10%
(g) New vessels at disc 6%
(h) Cataract complicated 6%
(i) Old iritis 4%



VII Result of investigations

		POSITIVE	NEGATIVE
1	Mantoux skin test 1 in 100 000	14 CASES 70%	6 CASES 30%
2	X ray of thorax	FIBROTIC LESION 3 30	7- 70%
3	E S R (Westergren)	HIGH - 2 %	NORMAL 25 78%
4	Nasal allergy	3 10	[illegible]9 90%
5	Septic tooth septal ulcer	3 10%	29 90%
6	Blood tests for syphilis (K B & W R)	[illegible] 7%	30 93%

RETINAL DETACHMENTS

As its incidence was found fairly high (13%) six cases of retinal detachments were further scrutinised In all cases detachment were localised in the lower half of the globe irrespective of the situation of the vascular lesion No definite tear could be detected in any one of them In two of them bands of retinitis proliferans were noted and in one an old patch of choroiditis was associated Detachment appeared late in the course of the disease

TREATED DETACHMENTS

Three cases were operated upon and surface diathermy was applied with penetrating diathermy to drain out fluid Case No 1 showed postoperative small haemorrhage at 12 O clock position followed by profuse vitreous haemorrhage after a few weeks Case No 2 also developed postoperative vitreous haemorrhage Case No 3 developed postoperative profuse vitreous opacities and ended in endophthalmitis

UNTREATED DETACHMENTS

Three detachments were only treated conservatively Case No 1 detachment became total Case No 2 retina flattened after a month Case No 3 remained unchanged

SURFACE DIATHERMY OF BLEEDING VESSELS

Diathermy coagulation of bleeding areas of retina is a known method of treatment to stop further bleeding (Weve 1935 1939, Franceschetti A and Forni S (1954a) Four cases were selected for this purpose A surface diathermy just to produce visible whitening of the fundus was applied over the area of affection about one fourth circumference of the eye between the equator and ora serrata under conjunctival flap Good results were obtained In all cases bleeding was arrested blood showed absorption and in none recurrence of haemorrhage has occurred yet

CASES NOT TREATED BY SURFACE DIATHERMY

The remaining 39 cases which had no surface diathermy but were treated by conservative method showed the following results

(a) blood showed quick absorption — 17 eyes—43 per cent
(b) no change in 12 eyes — 30 per cent
(c) fresh haemorrhage in subsequent attack — 10 eyes — 25 per cent

COAGULATION BY LIGHT

A light coagulation is of great help in preventing haemorrhage in vitreous as any area of periphlebitis can be coagulated long before the haemorrhage takes place

CONCLUSION

Incidence of Eales s disease is fairly high in Bengal Apart from high incidence of positive mantoux test no other positive etiological finding had any significant incidence

Among the treatments heat coagulation of diseased vessels proved to be of some value Diathermy treatment in retinal detachments however proved unsatisfactory

SUMMARY

46 eyes of Eales' disease were abalysed regarding incidence age frequency, sex ocular preponderance and results of conservative therapy and special therapy including surface diathermy to stop bleeding vessels and surface diathermy to treat detachment of retina

Diathermy treatment for retinal detachment was not found favourable but that for bleeding vessels showed satisfactory results

ACKNOWLEDGEMENT

I am grateful to Prof Dr K L Sen, Director, Institute of Ophthalmology, Medical College, Calcutta for guidance and help

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